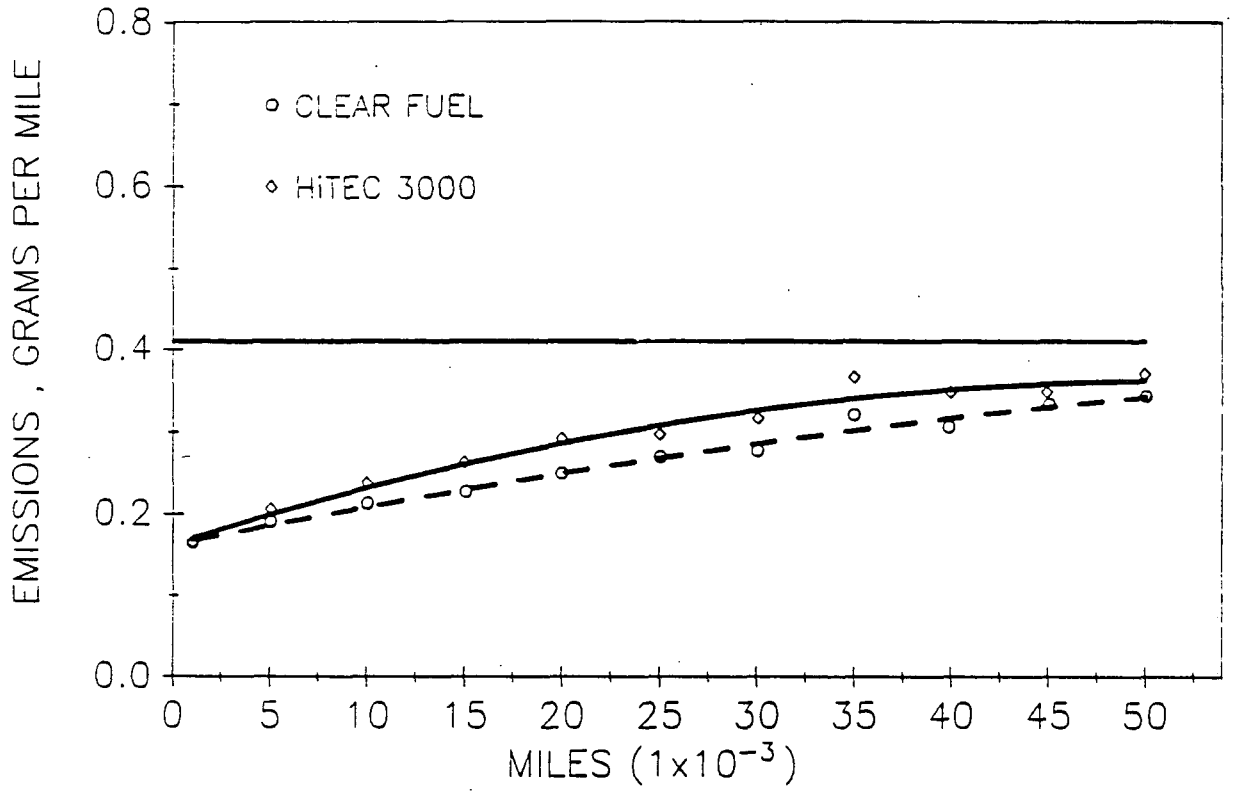


Figure 2-1. Quadratic trend of HC emissions averaged across all car models.

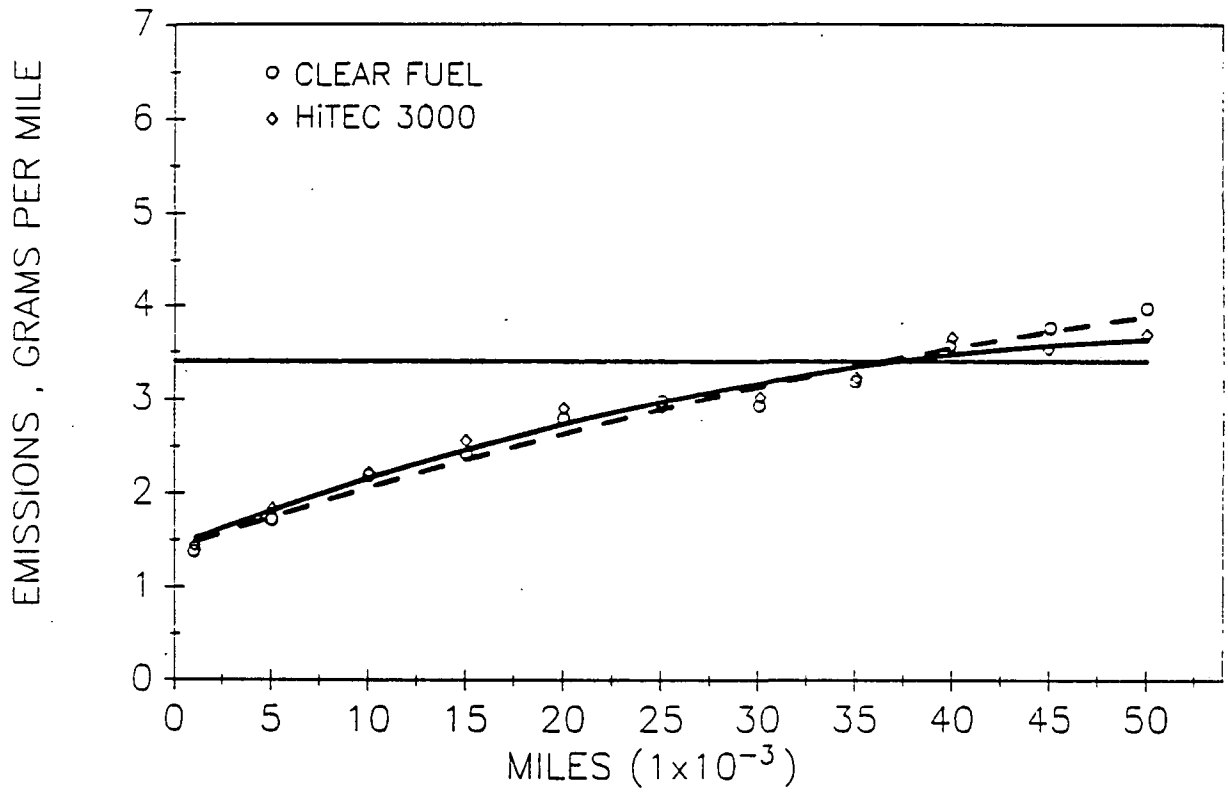


Figure 2-2. Quadratic trend of CO emissions averaged across all car models.

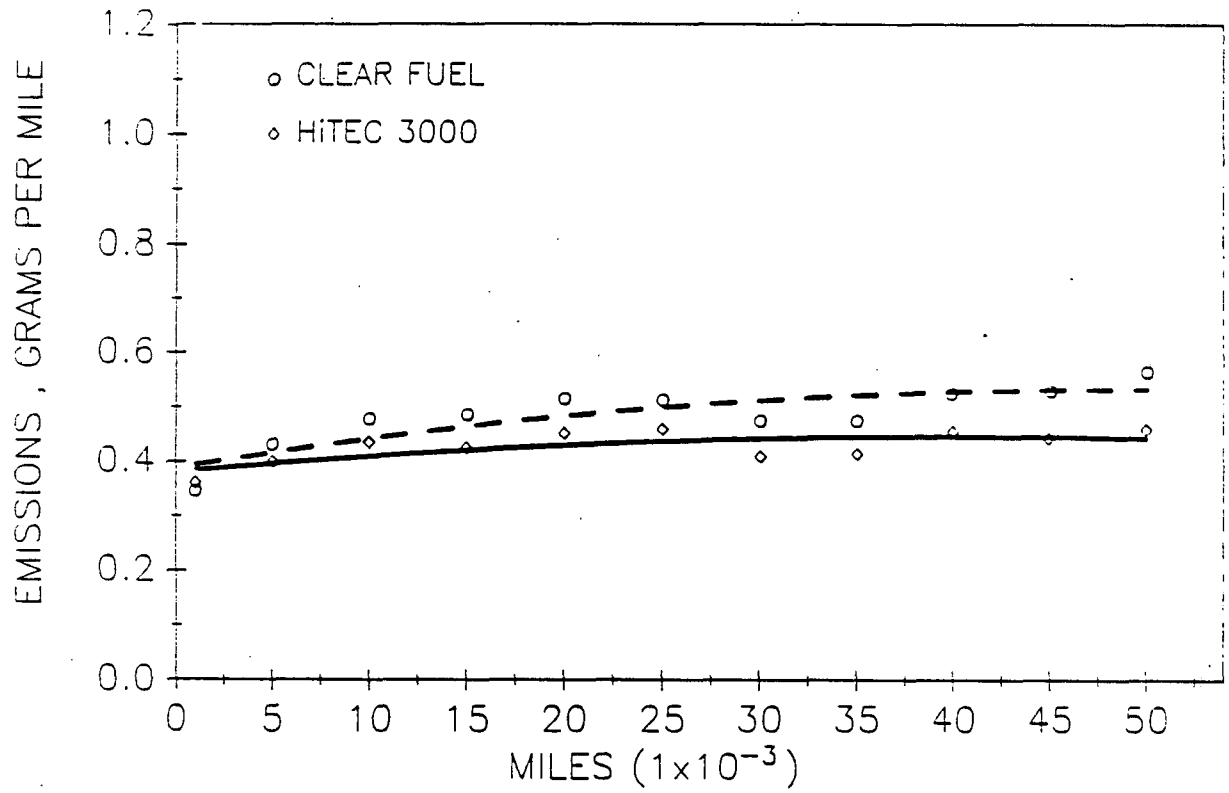


Figure 2-3. Quadratic trend of NO_x emissions averaged across all car models.

2.3.2 Exceedance Mileage

The next analysis variable we examine is CROSS, which is defined to be the mileage at which a car is predicted to exceed a tailpipe emission standard. In this analysis, we identify cars that are predicted to exceed one or more of the emission standards and then determine if clear fuel or HiTEC 3000 is associated with those exceedances.

There are three car models (i.e., T, F, and D) whose quadratic functions exceed the 0.41 gpvm HC standard. We compute the mileage at which each car is predicted to exceed the standard. We are able to conduct a fairly robust analysis because for each car model either: (1) no cars exceeded the standard or (2) all six cars exceeded the standard within (or very shortly after) the 0 to 50,000 mile interval.

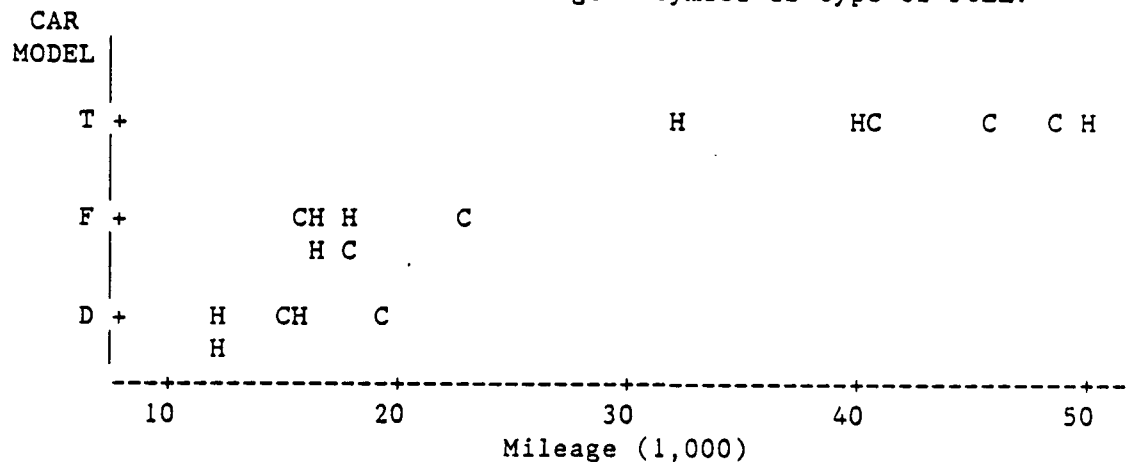
Table 2-5 presents a listing and plot of the data using only the three car models whose quadratic functions exceed the 0.41 gpvm standard. [One of the Model T cars actually exceeds the standard just beyond 50,000 miles; however, its omission would bias the results.] In Table 2-5, the columns "A", "B", and "C" are the constant, linear, and quadratic coefficients of each trend curve.

Note from the plot (shown at the bottom of Table 2-5) the variation in exceedance mileages -- even within car model. Our analysis indicates that this variability renders the exceedance mileages for the two fuels indistinguishable. In other words, HiTEC 3000 does not appear to cause or contribute to exceedances of the HC emission standard. The error mean squares suggest that the three car models should not be pooled (see Attachment 2B-4), but even pooling Models D, T, and F does not produce significant effects in

TABLE 2-5. QUADRATIC TRENDS FOR EACH CAR THAT EXCEEDS HC EMISSION STANDARD.

Car Model	Car Number	Fuel	Exceedance Mileage	Coefficients A	B	C
D	6	HiTEC	11,836	0.21670	0.018321	-.00016810
D	4	HiTEC	12,278	0.17097	0.023064	-.00029282
D	2	Clear	14,954	0.19723	0.016527	-.00015371
D	5	HiTEC	15,512	0.28916	0.006831	0.00006184
F	5	Clear	15,626	0.20321	0.014897	-.00010642
F	1	HiTEC	16,274	0.21383	0.013786	-.00010640
F	2	HiTEC	16,632	0.19527	0.014702	-.00010774
F	3	HiTEC	17,780	0.19722	0.013129	-.00006533
F	6	Clear	17,835	0.22361	0.009759	0.00003881
D	1	Clear	18,950	0.23215	0.010491	-.00005835
F	4	Clear	22,581	0.17750	0.010728	-.00001912
T	1	HiTEC	32,307	0.22855	0.005537	0.00000246
T	4	HiTEC	39,663	0.24759	0.003929	0.00000417
T	3	Clear	40,748	0.21584	0.002796	0.00004832
T	2	Clear	45,494	0.24592	-0.000947	0.00010010
T	6	Clear	48,559	0.21737	0.002636	.00002741
T	5	HiTEC	50,098	0.22248	0.005533	-.00003573

Plot of Exceedance Mileage. Symbol is type of FUEL.



exceedance mileages. We suspect that this is due in part to the large component of the error sum of squares coming from the Model T cars.

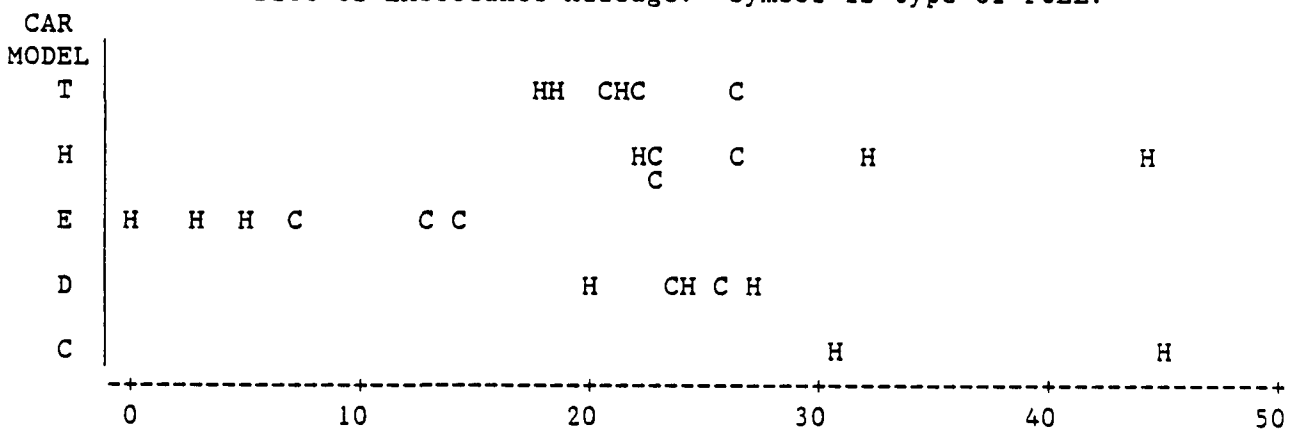
Table 2-6 presents a listing and plot of exceedance mileage for those cars that are predicted to exceed the CO emission standard. Car C-3, which was an HiTEC 3000 car, just exceeded the CO emission standard at about 31,000 miles. Predicted emissions peaked at 3.43 gpvm, and emissions dropped below the standard at about 40,000 miles. Car C-2, also an HiTEC 3000 car, exceeded the CO standard at approximately 46,000 miles; emissions peaked at 3.47 gpvm. No other model C car exceeded the standard. Thus, there is no comparison of clear fuel to HiTEC 3000 for model C, and these data points (i.e., for Cars C-2 and C-3) will not affect our CO analysis.

All individual cars within models D, E, H, and T eventually exceed the CO emission standard. For the other car models (i.e., C, F, G, and I), all test cars stayed below the standard throughout the test. A statistical representation without interaction (i.e., an overall effect rather than a car specific fuel effect) suggests a strong effect of car model and no difference between clear fuel and HiTEC 3000. However, a representation allowing interaction indicates that there are car-specific effects. These effects are broken out by a representation calling for a fuel comparison within each model of car. The computer output for this analysis is presented as Attachment 2B-5.

TABLE 2-6. QUADRATIC ANALYSIS OF EACH CAR THAT EXCEEDS CO EMISSION STANDARD.

Car Model	Car Number	Fuel	Exceedance Mileage
E	5	HiTEC	0
E	1	HiTEC	2,823
E	6	HiTEC	4,734
E	3	Clear	7,470
E	2	Clear	13,192
E	4	Clear	14,585
T	5	HiTEC	17,626
T	4	HiTEC	18,540
D	6	HiTEC	19,936
T	6	Clear	20,475
T	1	HiTEC	21,363
H	6	HiTEC	21,908
T	3	Clear	22,098
H	1	Clear	22,177
H	5	Clear	22,942
D	2	Clear	23,292
D	5	HiTEC	24,326
D	1	Clear	25,911
T	2	Clear	26,567
H	2	Clear	26,724
D	4	HiTEC	26,790
C	3	HiTEC	30,844
H	3	HiTEC	32,091
H	4	HiTEC	44,396
C	2	HiTEC	46,430

Plot of Exceedance Mileage. Symbol is type of FUEL.



From Attachment 2B-4 we see that HiTEC_CLR has a negative coefficient 4.615··· for car Model E and a positive coefficient -4.425··· for car Model H. In this particular statistical representation, the coefficient is multiplied by HiTEC_CLR, which is 1 for clear fuel and -1 for HiTEC 3000. Thus, this representation predicts a difference in exceedance mileage equal to twice the coefficient. Specifically, this representation predicts that Model E cars with clear fuel will exceed the CO standard 2 x 4.615 = 9,230 miles after HiTEC 3000 cars exceed the standard. On the other hand, an opposite and almost equal effect is observed for Model H cars. That is, Model H cars with clear fuel will exceed the CO standard 2 x 4.425 = 8,850 miles before HiTEC 3000 cars exceed the standard. No other car models show statistically significant effects. Thus, on balance, these effects tend to negate one another.

The quadratic trends for only two individual cars exceed the NO_x emission standard of 1.0 gpvm. Car T-6 is predicted to exceed the standard at 0 miles but is predicted to cross below the standard after about 12,000 miles. Car F-4 starts below the standard, but is predicted to exceed the standard at about 34,000 miles. Both cars T-6 and F-4 burned clear fuel; however, we cannot attribute statistical significance to this observation. That is, when an individual car is predicted to exceed an emission standard, the probability is 0.5 that the car is burning clear fuel. The occurrence of two events, each having a probability of 0.5, is not statistically significant. When only cars burning one type of fuel exceed the standard, at least 5 cars must exceed the standard in order to have statistical significance at or above the 95 percent level.

3. ANALYSIS OF 75,000-MILE DATA

In this section of the report, we repeat the analysis described in Section 2 for the 75,000-mile emission test data.

3.1 SIMPLE STATISTICS

For the 75,000-mile data there are 128 t-tests (8 car models x 16 mileage intervals) for each of the three pollutants. We present the results of the t-tests in Tables 3-1A, 3-1B, and 3-1C for those cars where emissions are statistically different between HiTEC 3000 and clear fuel.

Referring to Table 3-1A, we see that there are 32 cases where HiTEC 3000 results in statistically significant, higher HC emissions than does clear fuel, and one case where clear fuel results in higher HC emissions. If there were no true differences between the two fuels, natural sampling variability would lead us to expect about seven cases (0.05 x 128 = 6.4) in each of the two categories. Thus, HiTEC 3000 appears to result in slightly higher HC emissions than clear fuel, and this effect also appears to be a function of the car model being examined. That is, four car models (C, E, G, and T) account for 27 of the 32 t-tests in which HiTEC 3000 results in statistically significant, higher HC emissions. Also note that only seven of the 32 significant t-tests occur after the 50,000-mile interval.

Referring to Table 3-1B, we see that there are nine cases (out of 128 t-tests) where HiTEC 3000 results in significantly higher CO emissions than does clear fuel; however, there are 21 cases where clear fuel results in higher CO emissions. Again, if there were no fuel effect on emissions, natural sampling

TABLE 3-1A. T-TESTS FOR STATISTICALLY SIGNIFICANT DIFFERENCES IN HC EMISSIONS.

T-Test Number	Car Model	Mileage Interval	Mean Emissions (gpvm) Clear	Mean Emissions (gpvm) HiTEC 3000	T-Test [Clear-HiTEC 3000]	P-Value
1	C	15	0.15750	0.20400	-3.2088	0.01631
2	C	20	0.18950	0.23933	-7.0825	0.00105
3	C	25	0.17900	0.21400	-3.3627	0.01412
4	C	30	0.17492	0.21997	-3.3485	0.01430
5	C	40	0.17517	0.23900	-3.7623	0.00987
6	C	70	0.20767	0.25383	-3.2491	0.01570
7	D	20	0.44100	0.51917	-2.9177	0.03080
8	E	5	0.13067	0.16100	-4.6893	0.00469
9	E	10	0.15450	0.18067	-2.8030	0.02433
10	E	15	0.14767	0.19000	-2.9820	0.02033
11	E	20	0.15567	0.20217	-3.6073	0.01131
12	E	30	0.17108	0.19483	-2.4518	0.03515
13	F	20	0.39900	0.42183	-2.7618	0.02538
14	G	15	0.10550	0.14150	-5.4170	0.00281
15	G	20	0.13550	0.17150	-3.9675	0.00829
16	G	25	0.14033	0.17333	-2.5460	0.03179
17	G	35	0.13550	0.18183	-3.2254	0.01606
18	G	40	0.13917	0.18217	-2.2721	0.04276
19	G	45	0.13767	0.17067	-2.1752	0.04763
20	G	60	0.12975	0.16875	-3.1060	0.01801
21	G	65	0.14817	0.18900	-2.1480	0.04910
22	G	70	0.16367	0.18617	-2.1820	0.04727
23	G	75	0.16067	0.19733	-2.4431	0.03549
24	H	35	0.32083	0.27450	2.6704	0.97211
25	I	40	0.17583	0.19417	-2.1730	0.04775
26	I	45	0.17783	0.20250	-2.5196	0.03269
27	I	65	0.18117	0.20017	-2.2240	0.04510
28	T	10	0.24450	0.29717	-10.5799	0.00023
29	T	20	0.27967	0.32833	-2.2226	0.04518
30	T	25	0.30483	0.34600	-2.4147	0.03659
31	T	30	0.30175	0.37175	-3.2845	0.01519
32	T	35	0.33500	0.39800	-3.0037	0.01990
33	T	60	0.36617	0.41039	-5.7832	0.00222

TABLE 3-1B. T-TESTS FOR STATISTICALLY SIGNIFICANT DIFFERENCES IN CO EMISSIONS.

T-Test Number	Car Model	Mileage Interval	Mean Emissions (gpvm) Clear	Mean Emissions (gpvm) HiTEC 3000	T-Test [Clear-HiTEC 3000]	P-Value
1	D	55	5.39150	4.18050	3.1669	0.97470
2	D	60	6.36050	5.19508	3.0985	0.97332
3	E	5	2.65517	3.48400	-4.1926	0.00689
4	E	10	3.54217	4.07083	-5.0318	0.00366
5	E	15	3.77750	4.75083	-2.9946	0.02008
6	E	20	3.93933	4.82150	-2.5233	0.03256
7	E	30	4.30783	4.91558	-2.5069	0.03314
8	E	35	3.87117	4.89633	-3.5325	0.01209
9	E	45	6.18067	5.37867	3.7233	0.98979
10	E	50	6.42067	5.62533	5.2286	0.99681
11	E	55	6.07333	5.24217	2.7467	0.97423
12	F	15	1.29083	0.97033	2.9148	0.97827
13	F	20	1.18383	0.99483	3.1811	0.98325
14	F	25	1.61417	0.96167	4.1911	0.99310
15	F	30	1.88783	1.15792	10.3536	0.99975
16	F	35	1.70867	1.18483	3.3788	0.98609
17	F	40	1.84733	1.24500	4.5117	0.99464
18	F	45	2.18500	1.21717	7.8966	0.99930
19	F	50	2.54333	1.68183	4.7058	0.99537
20	F	60	2.81217	1.68075	8.3326	0.99943
21	F	65	3.00500	1.61783	6.2657	0.99834
22	F	70	2.90325	1.59500	11.1185	0.99600
23	F	75	2.22600	1.34825	17.6613	0.99840
24	G	60	2.05275	2.52475	-2.6848	0.02748
25	H	35	4.14100	3.36983	2.1447	0.95072
26	H	50	4.50717	3.94050	2.3779	0.96192
27	T	5	2.26850	2.65867	-2.2654	0.04308
28	T	10	2.37800	2.84950	-4.1266	0.00727
29	T	70	6.01267	5.43833	3.5950	0.98857
30	T	75	5.91283	4.74667	3.5485	0.98809

TABLE 3-1C. T-TESTS FOR STATISTICALLY SIGNIFICANT DIFFERENCES IN NOX EMISSIONS.

T-Test Number	Car Model	Mileage Interval	Mean Emissions (gpvm) Clear	Mean Emissions (gpvm) HiTEC 3000	T-Test [Clear-HiTEC 3000]	P-Value
1	C	35	0.37083	0.22367	3.3740	0.98603
2	C	40	0.38233	0.22600	3.9062	0.99128
3	C	45	0.51117	0.33667	2.4035	0.96296
4	C	55	0.56117	0.35517	2.4173	0.96351
5	C	60	0.63392	0.39175	2.9712	0.97945
6	C	65	0.52150	0.34350	2.9223	0.97843
7	C	75	0.63683	0.40367	2.3639	0.96133
8	D	25	0.33200	0.40833	-4.9357	0.00797
9	D	50	0.37750	0.48050	-13.1758	0.00047
10	D	55	0.54975	0.48433	5.1015	0.99272
11	D	60	0.62712	0.56558	4.4419	0.98939
12	E	5	0.26850	0.21417	2.8802	0.97750
13	E	10	0.35467	0.25667	5.1795	0.99670
14	F	10	0.73483	0.66100	2.4188	0.96357
15	F	15	0.83267	0.70100	2.8756	0.97739
16	F	20	0.81033	0.66900	3.9606	0.99167
17	F	25	0.82667	0.69317	2.8260	0.97623
18	F	30	0.89583	0.63050	5.7267	0.99770
19	F	35	0.93417	0.66783	2.7665	0.97474
20	F	40	0.93250	0.67867	3.0256	0.98053
21	F	45	0.91233	0.67233	2.3932	0.96255
22	F	65	1.65717	0.83500	2.3963	0.96267
23	F	75	1.71000	0.77200	7.8980	0.99217
24	G	1	0.14200	0.17333	-2.7837	0.02481
25	G	55	0.37700	0.33900	2.6017	0.97003
26	G	65	0.44267	0.35267	2.3635	0.96132
27	H	50	0.45300	0.35100	2.8418	0.97661
28	H	55	0.42133	0.31017	3.0423	0.98084
29	H	60	0.42525	0.31967	3.5761	0.98838
30	H	65	0.42700	0.31767	2.8499	0.97680
31	H	70	0.42317	0.29283	4.5242	0.99469
32	H	75	0.44100	0.28633	24.4555	0.99999
33	I	60	0.46425	0.30975	2.1494	0.95098
34	T	10	0.82717	0.48933	2.2370	0.95554
35	T	15	0.84833	0.48317	4.2123	0.99322
36	T	20	0.83817	0.47683	9.3873	0.99964
37	T	25	0.71383	0.46700	6.7075	0.99871
38	T	30	0.62450	0.47583	3.3731	0.98602
39	T	35	0.76017	0.53067	3.3880	0.98621
40	T	40	0.80550	0.64367	4.4607	0.99442
41	T	50	0.77867	0.62917	2.1485	0.95093
42	T	60	0.88811	0.71800	2.1815	0.95271
43	T	70	0.88733	0.65983	4.6198	0.99506
44	T	75	0.88400	0.65633	5.0721	0.99644

variability would lead us to expect about seven cases in each of the two categories. HiTEC 3000 appears to yield significantly lower CO emissions than clear fuel in Model F cars and in the later mileage intervals of Model E and T cars. HiTEC 3000 appears to yield statistically significant, higher CO emissions than clear fuel in the very early mileage intervals of Model T cars and in early mileage intervals of Model E cars. Thus, the CO comparison for the two fuels appears to be a function of car model being examined, and for Models E and T, a function of accumulated mileage.

Referring to Table 3-1C, we see that there are three cases where HiTEC 3000 results in statistically significant, higher NO_x emissions than clear fuel, but 41 cases where HiTEC 3000 results in lower NO_x emissions than clear fuel. HiTEC 3000 appears to yield statistically significant lower NO_x emissions than clear fuel consistently in Models T and F and sometimes in Models C, H, and E. We also note that the number of cases where HiTEC 3000 results in lower NO_x emissions than clear fuel for the 75,000-mile data is almost twice that observed for the 50,000-mile data (i.e., 41 versus 22).

3.2 ANALYSIS OF VARIANCE (ANOVA)

3.2.1 ANOVA By Mileage Interval

In this analysis we pool the emission data by mileage interval and fit a statistical model to the data that incorporates the effects of car model and fuel type. This particular statistical model does not allow fuel effects to be car-model specific. That is, the statistical model does not include a term for potential Model x Fuel interaction.

In exercising the above-described statistical model, we obtain an estimate of emissions for the clear fuel fleet and for the HiTEC 3000 fleet at each mileage interval. We compute the difference in emissions and the P-values at each mileage interval to determine if the differences are statistically different from zero. Since the statistical model estimates average emissions at each mileage interval for each car model, we can also determine which car models and fuel types are predicted to exceed the tailpipe emission standards at each mileage interval.*

Table 3-2A lists the mileages, the differences between clear fuel and HiTEC 3000 hydrocarbon emissions, the P-value for testing whether the true difference between clear fuel and HiTEC 3000 emissions is zero, and the car models that the underlying statistical model predicts to exceed the 0.41 gpvm HC emission standard. Table 3-2A shows that HC emissions are lower for clear fuel than for HiTEC 3000 at every mileage interval. However, note that the differences in HC emissions are <u>not</u> statistically significant at 1,000 miles nor from 45,000 miles through the completion of the test program (i.e., 75,000 miles).

Lastly, Table 3-2A shows that four car models are predicted to exceed the 0.41 gpvm HC standard. Since three car models (D, F, and T) are predicted to exceed the standard prior to 50,000 miles, the discussion presented in Section 2 need not be repeated here. Model H is predicted to exceed the HC standard at 60,000 and 65,000 miles for both clear fuel and HiTEC 3000.

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* For purposes of this analysis, the applicable emission standards are assumed to apply beyond 50,000 miles of vehicle operation.

TABLE 3-2A. MODELING RESULTS FOR HC EMISSIONS AS A FUNCTION OF MILEAGE.

Mileage	Difference in HC Emissions for Test Fleet [Clear-HiTEC 3000]	P-Value	MSE	Car Models Predicted to Exceed HC Standards	
				HiTEC 3000	Clear Fuel
1	0.000000	1.0000	.0002	--	--
5	-0.014937	0.0036	.0003	--	--
10	-0.019303	0.0018	.0004	--	--
15	-0.029389	0.0002	.0006	D F	--
20	-0.032910	0.0001	.0005	D F	D
25	-0.014974	0.1274	.0011	D F	D F
30	-0.034198	0.0002	.0008	D F	D F
35	-0.027842	0.0053	.0010	D F	D F
40	-0.028818	0.0162	.0015	D F T	D F T
45	-0.007585	0.6032	.0024	D F T	D F T
50	-0.013526	0.4046	.0030	D F T	D F T
55	-0.000662	0.9517	.0014	D F T	D F T
60	-0.020644	0.0867	.0016	D F H	D F H
65	-0.016701	0.4038	.0046	D F T H	D F T H
70	-0.013569	0.2503	.0015	D F	D F
75	-0.016991	0.2922	.0028	D F T	D F

We repeat the above-described analysis for CO and report the results in Table 3-2B. We observe statistically significant differences at 45,000, 50,000, 55,000, 60,000, and 70,000 miles with clear fuel having higher CO emissions than HiTEC 3000. Comparing these results with those presented in Table 2-2B, we observe the following trend with respect to increasing mileage. The difference between HiTEC 3000 CO emissions and clear fuel CO emissions appears to increase with increasing mileage -- with HiTEC 3000 emissions being lower than clear fuel emissions. The differences are statistically significant for three of the five high mileage intervals and almost significant at a fourth mileage interval (i.e., P-value = 0.0707 at 75,000 miles).

TABLE 3-2B. MODELING RESULTS FOR CO EMISSIONS AS A FUNCTION OF MILEAGE.

Mileage	Difference in CO Emissions for Test Fleet [Clear-HiTEC 3000]	P-Value	MSE	Car Models Predicted to Exceed CO Standards	
				HiTEC 3000	Clear Fuel
1	-0.06825	0.3312	.0577	--	--
5	-0.12450	0.1178	.0727	--	--
10	-0.03473	0.7107	.1010	E	E
15	-0.13855	0.2534	.1670	E	E
20	-0.09014	0.3602	.1108	E T	E
25	0.09498	0.3777	.1290	E T	E T
30	-0.06184	0.5556	.1265	E T D H	E T D H
35	-0.01173	0.9291	.2010	E T D H	E T D H
40	-0.03363	0.8119	.2305	E T D H	E T D H
45	0.26719	0.0481	.2002	E T D H	E T D H C
50	0.33801	0.0335	.2747	E T D H	E T D H
55	0.69408	0.0074	.7037	E T D H	E T D H
60	0.31420	0.0176	.1874	E T D H	E T D H
65	0.37085	0.1150	.6185	E T D H	E T D H
70	0.40591	0.0241	.3326	E T D H	E T D H
75	0.27042	0.0707	.2362	E T D H	E T D H

The results of the analysis for NO_x emissions are summarized in Table 3-2C. We observe that from 30,000 miles and beyond, clear fuel results in statistically higher NO_x emissions than does HiTEC 3000. We also note that the magnitude of the estimated differences in NO_x emissions continues to increase with increasing mileage.

TABLE 3-2C. MODELING RESULTS FOR NO_x EMISSIONS AS A FUNCTION OF MILEAGE.

Mileage	Difference in NO_x Emissions for Test Fleet [Clear-HiTEC 3000]	P-Value	MSE	Car Models Predicted to Exceed NO_x Standards	
				HiTEC 3000	Clear Fuel
1	-0.01471	0.5409	.0068	--	--
5	0.03227	0.2799	.0104	--	--
10	0.04963	0.1452	.0130	--	--
15	0.06369	0.0430	.0108	--	--
20	0.06196	0.0670	.0126	--	--
25	0.05151	0.0584	.0079	--	--
30	0.04909	0.0493	.0068	--	--
35	0.06719	0.0199	.0089	--	--
40	0.07268	0.0027	.0060	--	--
45	0.08494	0.0007	.0062	--	--
50	0.10390	0.0202	.0215	--	F
55	0.16036	0.0004	.0200	F	F
60	0.17143	0.0012	.0282	F	F
65	0.21201	0.0011	.0421	F	F
70	0.15446	0.0114	.0376	F	F
75	0.19634	0.0003	.0269	F	F

3.2.2 ANOVA Combining Mileage Intervals

In our next analysis, we combine the emission data across mileage intervals for each car. We subject the average emissions to an analysis of variance that tests whether average emissions are functions of fuel type and, if so, if the effect of fuel depends on car model.

We copy the type I sum of squares for each SAS® GLM run (see Table 3-3). The P-values indicate that the comparison of HiTEC 3000 to clear fuel is significant for HC and NO_x. The variable HiTEC_CLR is 1 if the fuel is HiTEC 3000 and -1 if the fuel is clear. The coefficient is a number added to HiTEC 3000 cars and subtracted from clear fuel cars so that twice this coefficient is the effect of a switch from clear fuel to HiTEC 3000, with a positive number indicating an increase due to HiTEC 3000. The P-values in

Table 3-3 for HiTEC_CLR*MODEL indicate that the difference is model specific for CO and NO_x but not for HC.

TABLE 3-3. ANOVA FOR COMBINED MILEAGE INTERVALS.

---------- Average HC Emissions ----------

Dependent Variable: MNHC

R-Square	C.V.	Root MSE	MNHC Mean
0.984272	7.423588	0.023240	0.31305335

Source	DF	Type I SS	Mean Square	F Value	Pr > F
MODEL	7	1.04145181	0.14877883	275.47	0.0001
HiTEC_CLR	1	0.00492396	0.00492396	9.12	0.0050
HiTEC_CLR*MODEL	7	0.00137541	0.00019649	0.36	0.9163

---------- Average CO Emissions ----------

Dependent Variable: MNCO

R-Square	C.V.	Root MSE	MNCO Mean
0.978032	7.181142	0.241137	3.35792417

Source	DF	Type I SS	Mean Square	F Value	Pr > F
MODEL	7	79.01855264	11.28836466	194.13	0.0001
HiTEC_CLR	1	0.27611553	0.27611553	4.75	0.0370
HITEC_CLR*MODEL	7	0.95581533	0.13654505	2.35	0.0479

---------- Average NO_x Emissions ----------

Dependent Variable: MNNOX

R-Square	C.V.	Root MSE	MNNOX Mean
0.917647	14.43242	0.073301	0.50788866

Source	DF	Type I SS	Mean Square	F Value	Pr > F
MODEL	7	1.57727461	0.22532494	41.94	0.0001
HiTEC_CLR	1	0.12837105	0.12837105	23.89	0.0001
HiTEC_CLR*MODEL	7	0.15034459	0.02147780	4.00	0.0032

The analysis summarized in Table 3-3 suggests that differences in emissions are car-model specific for average NO_x emissions and for average CO emissions; however, differences are not car-model specific for average HC emissions. We complete this part of the analysis by exercising the indicated statistical models. Using the SAS® Procedure GLM, the coefficient on HiTEC_Clear multiplied by 2 is our best estimate of the change in average emissions one

would expect by switching from clear fuel to HiTEC 3000. The SAS® computer outputs are provided as Attachments 2B-6, 2B-7, and 2B-8.

From Attachment 2B-6, we see that HiTEC 3000 increases average HC emissions by a statistically significant amount. Our best estimate of the increase is given by 2 x (.010256) = 0.021 gpvm. Attachment 2B-7 shows a statistically significant decrease in average CO emissions of 0.770 gpvm for Model F cars. Overall, the effect of switching from clear fuel to HiTEC 3000 is a decrease in average CO emissions of 0.155 gpvm. Attachment 2B-8 shows statistically significant differences in NO_x emissions for three car models. For these three car models (C, F, and T), average NO_x emissions are significantly lower for HiTEC 3000 than for clear fuel. The difference ranges from 0.135 to 0.333 gpvm. Overall, the effect of switching from clear fuel to HiTEC 3000 is a decrease in average NO_x emissions of 0.102 gpvm.

3.3 FITTING AND ANALYSIS OF QUADRATIC FUNCTIONS

In this phase of the analysis, we describe the pattern of emissions as a function of mileage using a simple polynomial. A quadratic equation captures the overall trend for the individual cars for all three pollutants. However, the degree of fit for the 75,000-mile data is not as good as for the 50,000-mile data. As with the 50,000-mile data analysis, we have omitted all 1,000-mile data for the purpose of fitting quadratic functions to the emission data.

The variable AVG represents average emissions and is equal to the integral of the quadratic function from 1,000 miles to 75,000 miles divided by the mileage interval (i.e., 74,000 miles). Average emissions for each car and each pollutant are summarized in Tables 3-4A, 3-4B, and 3-4C.

TABLE 3-4A. AVERAGE HC EMISSIONS DETERMINED FROM FITTED QUADRATICS.

Car Model	Car Number	Type of Fuel	Average Emissions (gpvm)
C	1	Clear	0.18531
C	4	Clear	0.16284
C	5	Clear	0.19340
C	2	HiTEC	0.21137
C	3	HiTEC	0.24245
C	6	HiTEC	0.20514
D	1	Clear	0.53672
D	2	Clear	0.54502
D	4	HiTEC	0.54688
D	5	HiTEC	0.56681
D	6	HiTEC	0.59099
E	2	Clear	0.24388
E	3	Clear	0.16963
E	4	Clear	0.16462
E	1	HiTEC	0.20747
E	5	HiTEC	0.20617
E	6	HiTEC	0.20175
F	4	Clear	0.47434
F	5	Clear	0.50089
F	6	Clear	0.54833
F	1	HiTEC	0.54127
F	2	HiTEC	0.50742
F	3	HiTEC	0.50608
G	1	Clear	0.13324
G	2	Clear	0.13542
G	4	Clear	0.13700
G	3	HiTEC	0.18348
G	5	HiTEC	0.15282
G	6	HiTEC	0.16125
H	1	Clear	0.30355
H	2	Clear	0.32442
H	5	Clear	0.30830
H	3	HiTEC	0.30034
H	4	HiTEC	0.28829
H	6	HiTEC	0.36773
I	1	Clear	0.19597
I	3	Clear	0.18538
I	5	Clear	0.17910
I	2	HiTEC	0.21245
I	4	HiTEC	0.18566
I	6	HiTEC	0.18887
T	2	Clear	0.33968
T	3	Clear	0.35899
T	6	Clear	0.34114
T	1	HiTEC	0.39045
T	4	HiTEC	0.36976
T	5	HiTEC	0.35993

TABLE 3-4B. AVERAGE CO EMISSIONS DETERMINED FROM FITTED QUADRATICS.

Car Model	Car Number	Type of Fuel	Average Emissions (gpvm)
C	1	Clear	2.67361
C	4	Clear	2.12968
C	5	Clear	2.80317
C	2	HiTEC	2.85124
C	3	HiTEC	2.99750
C	6	HiTEC	2.38793
D	1	Clear	4.29640
D	2	Clear	4.16479
D	4	HiTEC	3.89117
D	5	HiTEC	3.97372
D	6	HiTEC	4.42551
E	2	Clear	5.35159
E	3	Clear	5.00715
E	4	Clear	5.11753
E	1	HiTEC	5.37591
E	5	HiTEC	5.39423
E	6	HiTEC	5.04661
F	4	Clear	2.04602
F	5	Clear	1.97496
F	6	Clear	1.92064
F	1	HiTEC	1.26072
F	2	HiTEC	1.24079
F	3	HiTEC	1.20754
G	1	Clear	2.08284
G	2	Clear	1.95748
G	4	Clear	1.90162
G	3	HiTEC	2.01281
G	5	HiTEC	2.08121
G	6	HiTEC	1.98152
H	1	Clear	3.71730
H	2	Clear	3.57736
H	5	Clear	3.88732
H	3	HiTEC	3.43238
H	4	HiTEC	3.03003
H	6	HiTEC	3.80741
I	1	Clear	2.57055
I	3	Clear	2.58753
I	5	Clear	2.28933
I	2	HiTEC	2.67858
I	4	HiTEC	2.14449
I	6	HiTEC	2.29418
T	2	Clear	4.75260
T	3	Clear	4.95825
T	6	Clear	4.34551
T	1	HiTEC	4.92574
T	4	HiTEC	4.27613
T	5	HiTEC	4.28698

TABLE 3-4C. AVERAGE NO_x EMISSIONS DETERMINED FROM FITTED QUADRATICS.

Car Model	Car Number	Type of Fuel	Average Emissions (gpvm)
C	1	Clear	0.41329
C	4	Clear	0.51842
C	5	Clear	0.34160
C	2	HiTEC	0.32634
C	3	HiTEC	0.31236
C	6	HiTEC	0.26464
D	1	Clear	0.48391
D	2	Clear	0.44893
D	4	HiTEC	0.48632
D	5	HiTEC	0.50212
D	6	HiTEC	0.49522
E	2	Clear	0.43374
E	3	Clear	0.41009
E	4	Clear	0.37206
E	1	HiTEC	0.35408
E	5	HiTEC	0.37945
E	6	HiTEC	0.39078
F	4	Clear	1.22524
F	5	Clear	1.08125
F	6	Clear	0.88200
F	1	HiTEC	0.68679
F	2	HiTEC	0.82690
F	3	HiTEC	0.72276
G	1	Clear	0.36443
G	2	Clear	0.40406
G	4	Clear	0.38854
G	3	HiTEC	0.36760
G	5	HiTEC	0.34722
G	6	HiTEC	0.38014
H	1	Clear	0.35337
H	2	Clear	0.36219
H	5	Clear	0.49374
H	3	HiTEC	0.42715
H	4	HiTEC	0.48471
H	6	HiTEC	0.29587
I	1	Clear	0.39842
I	3	Clear	0.49204
I	5	Clear	0.47742
I	2	HiTEC	0.40685
I	4	HiTEC	0.31196
I	6	HiTEC	0.41132
T	2	Clear	0.80806
T	3	Clear	0.75626
T	6	Clear	0.83784
T	1	HiTEC	0.64212
T	4	HiTEC	0.56365
T	5	HiTEC	0.50427

Next we run a statistical model for AVG to determine if there are fuel effects and to determine if the fuel effects are car model specific or if there is a common fuel effect for all car models. [Note that the analysis presented in Section 3.2.1 did not allow for fuel effects to be car model specific.]

Table 3-5 summarizes these modeling results. The three rows of importance from Table 3-5 are those labeled "FUEL*MODEL".

TABLE 3-5. ANOVA ON AVERAGE EMISSIONS DETERMINED FROM FITTED QUADRATICS.

---------- Average HC Emissions ----------

Dependent Variable: AVG

Source	DF	Type I SS	Mean Square	F Value	Pr > F
FUEL	1	0.01109930	0.01109930	22.09	0.0001
MODEL	7	0.94474224	0.13496318	268.55	0.0001
FUEL*MODEL	7	0.00152918	0.00021845	0.43	0.8728

---------- Average CO Emissions ----------

Dependent Variable: AVG

Source	DF	Type I SS	Mean Square	F Value	Pr > F
FUEL	1	0.11923508	0.11923508	2.02	0.1654
MODEL	7	70.54738615	10.07819802	170.55	0.0001
FUEL*MODEL	7	0.92424015	0.13203431	2.23	0.0582

---------- Average NO_x Emissions ----------

Dependent Variable: AVG

Source	DF	Type I SS	Mean Square	F Value	Pr > F
FUEL	1	0.11847392	0.11847392	24.80	0.0001
MODEL	7	1.56312876	0.22330411	46.75	0.0001
FUEL*MODEL	7	0.14916989	0.02130998	4.46	0.0016

The first "FUEL*MODEL" row indicates that average HC emissions depend on fuel in a common way for all car models. That is, there is no significant interaction between fuel type and car model because the P-value is 0.8728. The second "FUEL*MODEL" row indicates that the interaction between fuel and car model is marginally significant (i.e., P-value = 0.0582). However, to maintain consistency with our definition of statistical significance (i.e., 95 percent probability limit), we will not include a term to account for interaction for average CO emissions. The last "FUEL*MODEL" row of Table 3-5 clearly shows that average NO_x emissions are dependent on fuel in a car-model specific way (i.e., P-value = 0.0016).

We complete this part of the analysis by estimating the effects of switching from clear fuel to HiTEC 3000 in an overall or model specific way. We run the above indicated statistical models (i.e., we do not need an interaction term for average HC and CO emissions, but we do need an interaction term for average NO_x emissions).

Our modeling results are presented as SAS® computer outputs and are provided as Attachments 2B-9, 2B-10, and 2B-11. Attachment 2B-9 shows that switching from clear fuel to HiTEC 3000 results in an increase in average HC emissions of 0.020 gpvm. This result is based on intergration of quadratic functions over the 1,000 to 75,000 mileage interval.

Attachment 2B-10 shows that switching from clear fuel to HiTEC 3000 results in a decrease in average CO emissions of 0.139 gpvm. Lastly, Attachment 2B-11 shows the effect of switching fuels in both a model specific way and as an overall effect. Switching from clear fuel to HiTEC 3000 results in an overall

decrease in average NO_x emissions of 0.097 gpvm. Note that the effect on two car models in much larger than the overall effect. Switching from clear fuel to HiTEC 3000 results in a decrease of 0.317 gpvm for Model F cars and a decrease of 0.231 gpvm for Model T cars.

We complete our analysis of average differences in emissions between HiTEC 3000 and clear fuel by summarizing, in Table 3-6, the results obtained from ANOVA on average values and from integration of quadratic functions. Even though the degree of quadratic fit for the 75,000-mile data is not as good as for 50,000-mile data, the agreement between the quadratic results and the results based on simply averaging the emission measurements is excellent. This suggests that our estimates of differences in average emissions between clear fuel and HiTEC 3000 is quite robust.

TABLE 3-6. AVERAGE DIFFERENCES IN EMISSIONS (gpvm) FOR 75,000 MILE-DATA -- HiTEC 3000 VERSUS CLEAR FUEL.

Pollutant	ANOVA on Average Values	Integration of Quadratic Functions
HC	0.021 Higher	0.020 Higher
CO	0.155 Lower	0.139 Lower
NO_x	0.102 Lower	0.097 Lower

Figures 3-1, 3-2, and 3-3 show the quadratic trend for each pollutant, averaged across all clear-fuel cars and across all HiTEC 3000 cars. The graphs also show the data points upon which the quadratic curves are based.

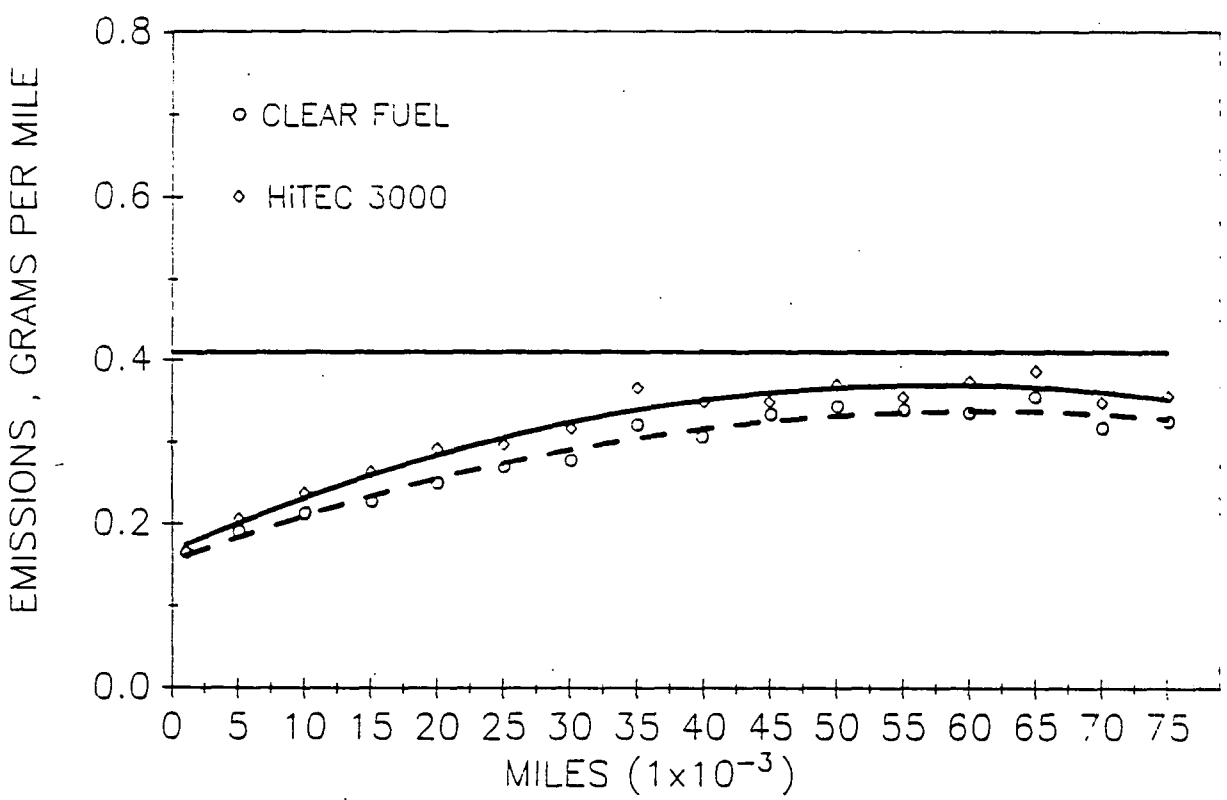

Figure 3-1. Quadratic trend of HC emissions averaged across all car models.

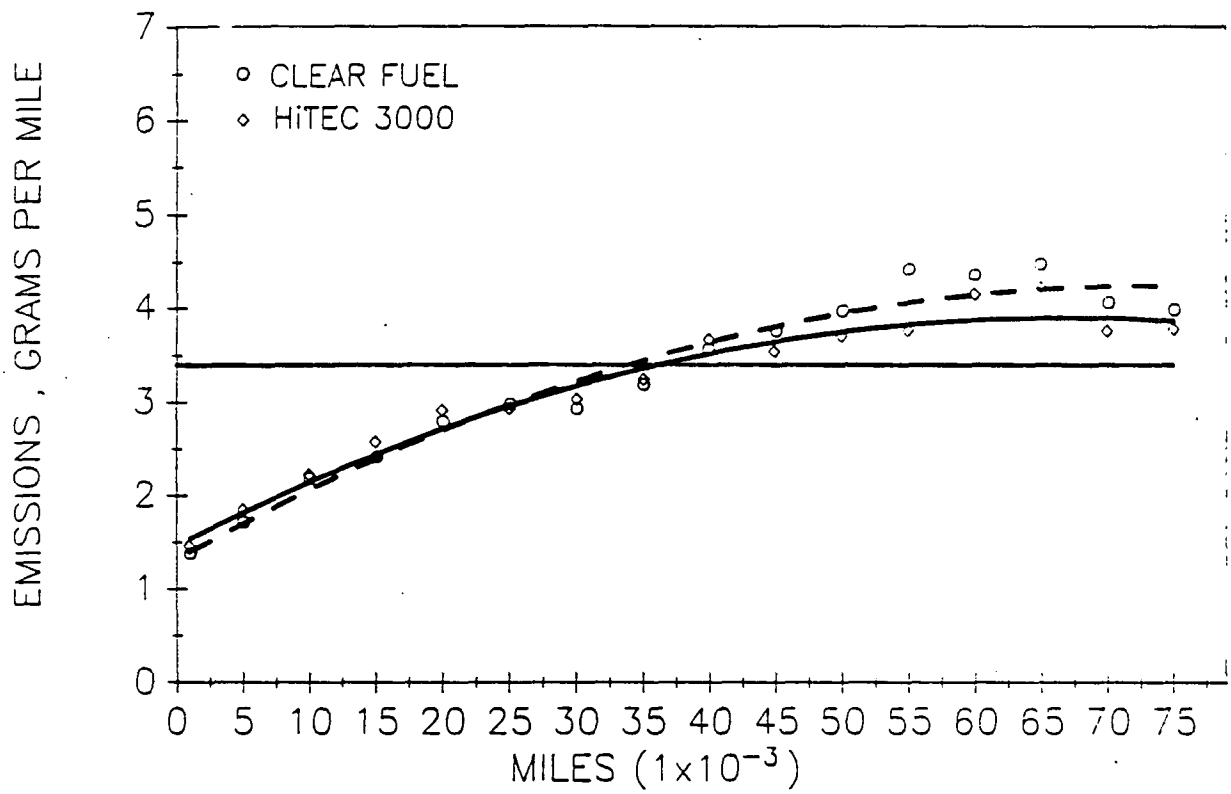

Figure 3-2. Quadratic trend of CO emissions averaged across all car models.

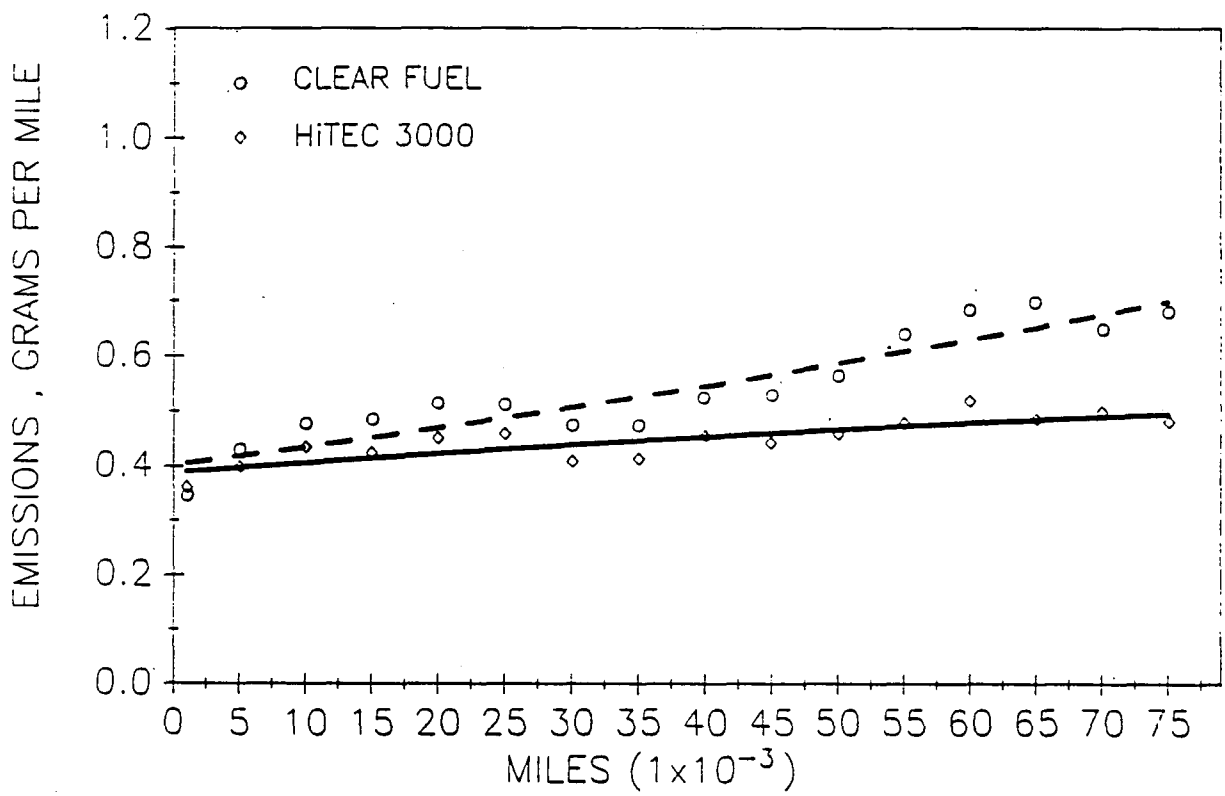

Figure 3–3. Quadratic trend of NO_x emissions averaged across all car models.

ATTACHMENTS

ATTACHMENT 2B-1. FITTED QUADRATICS FOR EACH CAR. AVG IS MEAN VALUE USING INTEGRATION OF FITTED CURVE ANALYSIS OF HC CURVE -- 50,000-MILE DATA.

Dependent Variable: AVG

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	8	0.76693310	0.09586664	241.94	0.0001
Error	38	0.01505733	0.00039625		
Corrected Total	46	0.78199043			

R-Square	C.V.	Root MSE	AVG Mean
0.980745	7.076021	0.019906	0.28131515

Parameter		Estimate		T for H0: Parameter=0	Pr > | T |	Std Error of Estimate
INTERCEPT		0.3332262642	B	41.00	0.0001	0.00812656
MODEL	C	-.1383102812	B	-12.03	0.0001	0.01149269
	D	0.1655117518	B	13.72	0.0001	0.01206767
	E	-.1535182253	B	-13.36	0.0001	0.01149269
	F	0.1439047148	B	12.52	0.0001	0.01149269
	G	-.1898710042	B	-16.52	0.0001	0.01149269
	H	-.0640160584	B	-5.57	0.0001	0.01149269
	I	-.1446385624	B	-12.59	0.0001	0.01149269
	T	0.0000000000	B	.	.	.
HiTEC_CLR		0.0113152295		3.89	0.0004	0.00290977

CONVERSION OF REGRESSION ESTIMATES TO DIFFERENCES.
DIFF IS PREDICTED DIFFERENCE BETWEEN FUELS (HiTEC_CLEAR).

EST	DIFF
0.011315	0.022630

ATTACHMENT 2B-2. FITTED QUADRATICS FOR EACH CAR. AVG IS MEAN VALUE USING INTEGRATION OF FITTED CURVE ANALYSIS OF CO CURVE -- 50,000-MILE DATA.

Dependent Variable: AVG

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	15	50.13920752	3.34261383	73.10	0.0001
Error	31	1.41743844	0.04572382		
Corrected Total	46	51.55664596			

R-Square	C.V.	Root MSE	AVG Mean
0.972507	7.454483	0.213831	2.86849239

Parameter		Estimate	T for H0: Parameter=0	Pr > | T |	Std Error of Estimate
INTERCEPT		3.777710547 B	43.27	0.0001	0.08729626
MODEL	C	-1.221311136 B	-9.89	0.0001	0.12345555
	D	-0.262948657 B	-2.01	0.0534	0.13094439
	E	0.856516430 B	6.94	0.0001	0.12345555
	F	-2.460786205 B	-19.93	0.0001	0.12345555
	G	-1.947566055 B	-15.78	0.0001	0.12345555
	H	-0.699753421 B	-5.67	0.0001	0.12345555
	I	-1.433402417 B	-11.61	0.0001	0.12345555
	T	0.000000000 B	.	.	.
HiTEC_CLR(Model)	C	0.093112285	1.07	0.2944	0.08729626
	D	0.019306710	0.20	0.8445	0.09760018
	E	0.240318999	2.75	0.0098	0.08729626
	F	-0.244346395	-2.80	0.0087	0.08729626
	G	-0.011980560	-0.14	0.8917	0.08729626
	H	-0.164323785	-1.88	0.0692	0.08729626
	I	-0.010415515	-0.12	0.9058	0.08729626
	T	0.067498123	0.77	0.4453	0.08729626

CONVERSION OF REGRESSION ESTIMATES TO DIFFERENCES.
DIFF IS PREDICTED DIFFERENCE BETWEEN FUELS (HiTEC_CLEAR).

MODEL	EST	DIFF
C	0.09311	0.18622
D	0.01931	0.03861
E	0.24032	0.48064
F	-0.24435	-0.48869
G	-0.01198	-0.02396
H	-0.16432	-0.32865
I	-0.01042	-0.02083
T	0.06750	0.13500

N Obs	Variable	Label	Mean
8	EST	regression coefficient = 1/2 effect	-0.0013538
	DIFF	effect of switch from clear to HiTEC	-0.0027075

ATTACHMENT 2B-3. FITTED QUADRATICS FOR EACH CAR. AVG IS MEAN VALUE USING INTEGRATION OF FITTED CURVE ANALYSIS OF NO_x CURVE -- 50,000-MILE DATA.

Dependent Variable: AVG

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	15	1.20391182	0.08026079	21.37	0.0001
Error	31	0.11644668	0.00375634		
Corrected Total	46	1.32035850			

R-Square	C.V.	Root MSE	AVG Mean
0.911807	13.21268	0.061289	0.46386519

Parameter		Estimate		T for H0: Parameter=0	Pr > | T |	Std Error of Estimate
INTERCEPT		0.6446544501	B	25.76	0.0001	0.02502114
MODEL	C	-.3318885855	B	-9.38	0.0001	0.03538523
	D	-.1815533998	B	-4.84	0.0001	0.03753171
	E	-.2938618918	B	-8.30	0.0001	0.03538523
	F	0.1167176865	B	3.30	0.0024	0.03538523
	G	-.2858262398	B	-8.08	0.0001	0.03538523
	H	-.2258241385	B	-6.38	0.0001	0.03538523
	I	-.2479011774	B	-7.01	0.0001	0.03538523
	T	0.0000000000	B			
HiTEC_CLR(MODEL)	C	-.0399361063		-1.60	0.1206	0.02502114
	D	0.0221777507		0.79	0.4339	0.02797448
	E	-.0109265829		-0.44	0.6654	0.02502114
	F	-.0874501672		-3.50	0.0015	0.02502114
	G	-.0045929742		-0.18	0.8556	0.02502114
	H	0.0279954801		1.12	0.2718	0.02502114
	I	-.0181719199		-0.73	0.4731	0.02502114
	T	-.1239915217		-4.96	0.0001	0.02502114

MODEL	EST	DIFF
C	-0.03994	-0.07987
D	0.02218	0.04436
E	-0.01093	-0.02185
F	-0.08745	-0.17490
G	-0.00459	-0.00919
H	0.02800	0.05599
I	-0.01817	-0.03634
T	-0.12399	-0.24798

N Obs	Variable	Label	Mean
8	EST	regression coefficient = 1/2 effect	-0.0293620
	DIFF	effect of switch from clear to HiTEC	-0.0587240

ATTACHMENT 2B-4. EXCEEDANCE MILEAGE ANALYSIS FOR HC EMISSIONS.

Dependent Variable: CROSS

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	3	2780.434490	926.811497	50.55	0.0001
Error	13	238.334496	18.333423		
Corrected Total	16	3018.768986			

R-Square	C.V.	Root MSE	CROSS Mean
0.921049	16.65194	4.281755	25.7132457

Source	DF	Type I SS	Mean Square	F Value	Pr > F
MODEL	2	2736.800669	1368.400334	74.64	0.0001
HiTEC_CLR	1	43.633821	43.633821	2.38	0.1469

Parameter		Estimate	T for H0: Parameter=0	Pr > |T|	Std Error of Estimate
INTERCEPT		42.81153242 B	24.49	0.0001	1.74801901
MODEL	D	-27.78340153 B	-10.68	0.0001	2.60113553
	F	-25.02371134 B	-10.12	0.0001	2.47207219
	T	0.00000000 B	.	.	.
HiTEC_CLR		-1.61159898	-1.54	0.1469	1.04464117

ATTACHMENT 2B-5. EXCEEDANCE MILEAGE ANALYSIS FOR CO EMISSIONS.

Dependent Variable: CROSS

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	8	2411.278014	301.409752	10.01	0.0001
Error	16	481.726008	30.107876		
Corrected Total	24	2893.004022			

R-Square	C.V.	Root MSE	CROSS Mean
0.833486	25.53376	5.487064	21.4894517

Source	DF	Type I SS	Mean Square	F Value	Pr > F
MODEL	4	2142.513569	535.628392	17.79	0.0001
HiTEC-CLR(MODEL)	4	268.764445	67.191111	2.23	0.1114

Parameter		Estimate	T for H0: Parameter=0	Pr > | T |	Std Error of Estimate
INTERCEPT		21.11142014 B	9.42	0.0001	2.24008465
MODEL	C	17.52541010 B	3.91	0.0012	4.48016931
	D	3.03109281 B	0.90	0.3804	3.36012698
	E	-13.97757222 B	-4.41	0.0004	3.16795810
	H	7.26146086 B	2.29	0.0358	3.16795810
	T	0.00000000 B	.	.	.
HiTEC_CLR(MODEL)	C	0.00000000 B	.	.	.
	D	-0.45882606 B	-0.18	0.8569	2.50449078
	E	-4.61489631 B	-2.06	0.0560	2.24008465
	H	4.42531013 B	1.98	0.0657	2.24008465
	T	-1.93520524 B	-0.86	0.4004	2.24008465

ATTACHMENT 2B-6. ANOVA ON CAR AVERAGES -- AVERAGE HC EMISSIONS.

Dependent Variable: MNHC

Parameter		Estimate	T for H0: Parameter=0	Pr > | T |	Std Error of Estimate
INTERCEPT		0.3658611111 B	41.04	0.0001	0.00891434
MODEL	C	-.1654300109 B	-13.12	0.0001	0.01260678
	D	0.2075991884 B	15.68	0.0001	0.01323751
	E	-.1627434641 B	-12.91	0.0001	0.01260678
	F	0.1658676471 B	13.16	0.0001	0.01260678
	G	-.2135811547 B	-16.94	0.0001	0.01260678
	H	-.0382854031 B	-3.04	0.0043	0.01260678
	I	-.1741972699 B	-13.82	0.0001	0.01260678
	T	0.0000000000 B	.	.	.
HiTEC_CLR		0.0102573259	3.21	0.0027	0.00319185

Changing regression coefficients to effects
Dependent Variable: MNHC

EST	DIFF
0.010257	0.020515

ATTACHMENT 2B-7. ANOVA ON CAR AVERAGES -- AVERAGE CO EMISSIONS.

Dependent Variable: MNCO

Parameter		Estimate	T for H0: Parameter=0	Pr > | T |	Std Error of Estimate
INTERCEPT		4.840699074 B	49.17	0.0001	0.09844390
MODEL	C	-2.191120098 B	-15.74	0.0001	0.13922069
	D	-0.498539760 B	-3.38	0.0020	0.14766584
	E	0.536423475 B	3.85	0.0005	0.13922069
	F	-3.187963126 B	-22.90	0.0001	0.13922069
	G	-2.806224673 B	-20.16	0.0001	0.13922069
	H	-1.136683007 B	-8.16	0.0001	0.13922069
	I	-2.397905399 B	-17.22	0.0001	0.13922069
	T	0.000000000 B	.	.	.
HiTEC CLR(MODEL)	C	0.107108388	1.09	0.2850	0.09844390
	D	-0.096884804	-0.88	0.3855	0.11006362
	E	0.032897059	0.33	0.7405	0.09844390
	F	-0.385115686	-3.91	0.0005	0.09844390
	G	0.040339325	0.41	0.6848	0.09844390
	H	-0.133115741	-1.35	0.1861	0.09844390
	I	-0.072910573	-0.74	0.4645	0.09844390
	T	-0.110819444	-1.13	0.2689	0.09844390

Changing regression coefficients to effects
Dependent Variable: MNCO

EST	DIFF
0.10711	0.21422
-0.09688	-0.19377
0.03290	0.06579
-0.38512	-0.77023
0.04034	0.08068
-0.13312	-0.26623
-0.07291	-0.14582
-0.11082	-0.22164

N Obs	Variable	Label	Mean
8	EST	regression coefficient = 1/2 effect	-0.0773127
	DIFF	effect of switch from clear to HiTEC	-0.1546254

ATTACHMENT 2B-8. ANOVA ON CAR AVERAGES -- AVERAGE NO_x EMISSIONS.

Dependent Variable: MNNOX

Parameter		Estimate		T for H0: Parameter=0	Pr > | T |	Std Error of Estimate
INTERCEPT		0.6954027778	B	23.24	0.0001	0.02992486
MODEL	C	-.3227766885	B	-7.63	0.0001	0.04232014
	D	-.2134003268	B	-4.75	0.0001	0.04488729
	E	-.2956576797	B	-6.99	0.0001	0.04232014
	F	0.2140354575	B	5.06	0.0001	0.04232014
	G	-.3132843137	B	-7.40	0.0001	0.04232014
	H	-.2961909041	B	-7.00	0.0001	0.04232014
	I	-.2791410335	B	-6.60	0.0001	0.04232014
	T	0.0000000000	B	.	.	.
HiTEC_CLR (MODEL)	C	-.0673837146		-2.25	0.0316	0.02992486
	D	0.0119289216		0.36	0.7238	0.03345701
	E	-.0134803922		-0.45	0.6555	0.02992486
	F	-.1665964052		-5.57	0.0001	0.02992486
	G	-.0107949346		-0.36	0.7207	0.02992486
	H	-.0070904139		-0.24	0.8143	0.02992486
	I	-.0444550313		-1.49	0.1475	0.02992486
	T	-.1082546296		-3.62	0.0010	0.02992486

Changing regression coefficients to effects
Dependent Variable: MNNOX

EST	DIFF
-0.06738	-0.13477
0.01193	0.02386
-0.01348	-0.02696
-0.16660	-0.33319
-0.01079	-0.02159
-0.00709	-0.01418
-0.04446	-0.08891
-0.10825	-0.21651

N Obs	Variable	Label	Mean
8	EST	regression coefficient = 1/2 effect	-0.0507658
	DIFF	effect of switch from clear to HiTEC	-0.1015316

ATTACHMENT 2B-9. FITTED QUADRATICS FOR EACH CAR. AVG IS MEAN VALUE USING INTEGRATION OF FITTED CURVE ANALYSIS OF HC CURVE -- 75,000-MILE DATA.

Dependent Variable: AVG

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	8	0.95584154	0.11948019	265.38	0.0001
Error	38	0.01710836	0.00045022		
Corrected Total	46	0.97294990			

R-Square	C.V.	Root MSE	AVG Mean
0.982416	6.943763	0.021218	0.30557477

Parameter		Estimate		T for H0: Parameter=0	Pr > | T |	Std Error of Estimate
INTERCEPT		0.3599930321	B	41.56	0.0001	0.00866237
MODEL	C	-.1599078072	B	-13.05	0.0001	0.01225044
	D	0.1952818745	B	15.18	0.0001	0.01286334
	E	-.1610736674	B	-13.15	0.0001	0.01225044
	F	0.1530623288	B	12.49	0.0001	0.01225044
	G	-.2094577741	B	-17.10	0.0001	0.01225044
	H	-.0445541013	B	-3.64	0.0008	0.01225044
	I	-.1687554718	B	-13.78	0.0001	0.01225044
	T	0.0000000000	B	.	.	.
HiTEC_CLR		0.0100510966	B	3.24	0.0025	0.00310163

CONVERSION OF REGRESSION ESTIMATES TO DIFFERENCES.
DIFF IS PREDICTED DIFFERENCE BETWEEN FUELS (HiTEC_CLEAR).

EST	DIFF
0.010051	0.020102

ATTACHMENT 2B-10. FITTED QUADRATICS FOR EACH CAR. AVG IS MEAN VALUE USING INTEGRATION OF FITTED CURVE ANALYSIS OF CO CURVE -- 75,000 MILE DATA.

Dependent Variable: AVG (almost inappropriate according to interaction test)

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	8	70.66662124	8.83332765	121.79	0.0001
Error	38	2.75609131	0.07252872		
Corrected Total	46	73.42271254			

R-Square	C.V.	Root MSE	AVG Mean
0.962463	8.266617	0.269312	3.25782084

Parameter		Estimate		T for H0: Parameter=0	Pr > | T |	Std Error of Estimate
INTERCEPT		4.590870181	B	41.76	0.0001	0.10994599
MODEL	C	-1.950348512	B	-12.54	0.0001	0.15548710
	D	-0.426624014	B	-2.61	0.0128	0.16326621
	E	0.624633046	B	4.02	0.0003	0.15548710
	F	-2.982425696	B	-19.18	0.0001	0.15548710
	G	-2.587954545	B	-16.64	0.0001	0.15548710
	H	-1.015570507	B	-6.53	0.0001	0.15548710
	I	-2.163426611	B	-13.91	0.0001	0.15548710
	T	0.000000000	B	.	.	.
HiTEC_CLR		-0.069642058		-1.77	0.0849	0.03936698

CONVERSION OF REGRESSION ESTIMATES TO DIFFERENCES.
DIFF IS PREDICTED DIFFERENCE BETWEEN FUELS (HiTEC_CLEAR).

EST	DIFF
-0.069642	-0.13928

ATTACHMENT 2B-11. FITTED QUADRATICS FOR EACH CAR. AVG IS MEAN VALUE USING INTEGRATION OF FITTED CURVE ANALYSIS OF NOX CURVE -- 75,000-MILE DATA.

Dependent Variable: AVG

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	15	1.83077257	0.12205150	25.55	0.0001
Error	31	0.14808528	0.00477694		
Corrected Total	46	1.97885785			

R-Square	C.V.	Root MSE	AVG Mean
0.925166	13.74265	0.069115	0.50292677

Parameter		Estimate		T for H0: Parameter=0	Pr > | T |	Std Error of Estimate
INTERCEPT		0.6853675779	B	24.29	0.0001	0.02821626
MODEL	C	-.3225909625	B	-8.08	0.0001	0.03990382
	D	-.2048811115	B	-4.84	0.0001	0.04232439
	E	-.2953325969	B	-7.40	0.0001	0.03990382
	F	0.2187898343	B	5.48	0.0001	0.03990382
	G	-.3100362825	B	-7.77	0.0001	0.03990382
	H	-.2825295261	B	-7.08	0.0001	0.03990382
	I	-.2690307482	B	-6.74	0.0001	0.03990382
	T	0.0000000000	B	.	.	.
HiTEC_CLR (MODEL)	C	-.0616610184		-2.19	0.0365	0.02821626
	D	0.0140692912		0.45	0.6587	0.03154674
	E	-.0152624831		-0.54	0.5924	0.02821626
	F	-.1586735180		-5.62	0.0001	0.02821626
	G	-.0103452733		-0.37	0.7164	0.02821626
	H	-.0002605160		-0.01	0.9927	0.02821626
	I	-.0396260755		-1.40	0.1701	0.02821626
	T	-.1153529630		-4.09	0.0003	0.02821626

CONVERSION OF REGRESSION ESTIMATES TO DIFFERENCES.
DIFF IS PREDICTED DIFFERENCE BETWEEN FUELS (HiTEC_CLEAR).

EST	DIFF
-0.06166	-0.12332
0.01407	0.02814
-0.01526	-0.03052
-0.15867	-0.31735
-0.01035	-0.02069
-0.00026	-0.00052
-0.03963	-0.07925
-0.11535	-0.23071

N Obs	Variable	Label	Mean
8	EST	REGRESSION ESTIMATE = 1/2 DIFFERENCE	-0.0483891
	DIFF	ESTIMATED DIFFERENCE HiTEC_CLEAR	-0.0967781

APPENDIX 2C

INSTANTANEOUS EFFECTS ANALYSIS

Summary

One of the criteria that the Administrator of the Environmental Protection Agency uses to evaluate the environmental effect of a potential gasoline additive is its instantaneous effect on the automobile's emission system. That is, does the additive cause a significant increase in pollutants emitted from the tailpipe as soon as the additive is introduced into the gasoline. HiTEC® 3000 Performance Additive ("HiTEC 3000") was tested for a possible instantaneous effect on the emission systems on automobiles with similar engine configurations to those in Ethyl Corporation's ("Ethyl") 48-car test fleet.

To determine whether the HiTEC 3000 additive contributes to an instantaneous increase in automotive emissions, Ethyl tested nine rental automobiles, with engine configurations similar to the eight models in its 48-car test fleet, for HC, CO, and NOx tailpipe emissions. Ethyl conducted these tests with a clear test fuel first and then with the same test fuel treated with the HiTEC 3000 additive. The test results indicated that there were no statistically significant differences between the emission levels of the two fuels.

Discussion

The Environmental Protection Agency requires that waiver applicants for additives in unleaded gasoline provide evidence that the additive does not cause a negative instantaneous effect on automotive exhaust emissions. In order to check for instantaneous effects, emission tests are conducted on a particular automobile with a control fuel and then with the waiver fuel using the same automobile.

Test Procedure - Ethyl leased nine automobiles that had the same engine configurations as the eight-engine model families in Ethyl's 48-car test fleet. The intention was to test only eight automobiles, one from each engine model in the test fleet. Ethyl actually tested nine automobiles because the first "D" model leased by Ethyl gave inconsistent test results for HC and NOx. A second "D" model was leased and emission ratings were obtained; however, the inclusion of the second "D" model in the data set did not change the outcome of the three statistical tests for instantaneous effects. A description of the automobiles used for the instantaneous emissions testing is given in Attachment 2C-1. The catalyst number for the second "D" model was not documented when Ethyl leased the vehicle so it does not appear in Attachment 2C-1.

Emission tests were performed according to FTP-75 guidelines. Each automobile was tested in triplicate with Howell EEE gasoline followed by triplicate ratings with Howell EEE gasoline containing 0.03125 gm Mn as the HiTEC 3000 additive. The automobiles were leased in Detroit, Michigan and testing was conducted by ECS Laboratories. The emission test data for HC, CO, and NOx for both fuels in the nine vehicles are shown in Attachment 2C-2.

Data Analysis - In prior waiver requests, the Environmental Protection Agency has used three different statistical procedures to check for instantaneous emission effects. These test procedures are the (1) paired difference test, (2) sign of difference test and (3) deteriorated emissions test. A description of the tests and results of the data analysis for the HiTEC 3000 additive follow.

(1) Paired Difference Test - For each vehicle, compute the mean difference between the control fuel and waiver fuel emissions for each pollutant. Then calculate a 90% confidence interval about the estimate for the true mean difference. This interval is expected to include the theoretical increase (or decrease) in emissions due to the additive. The instantaneous effect is regarded as adverse if the entire interval exceeds zero or if the upper bound exceeds 10% of the standard.

The statistical method used is an analysis of differences in average performance between two variables assuming the differences come from the same normal distribution. In this case, the two variables are the tailpipe emissions obtained with Howell EEE gasoline and with Howell EEE gasoline containing 0.03125 gm Mn as the HiTEC 3000 additive. The student's "t" statistic is used to calculate 90% confidence intervals. The variance "s_d^2" used in the analysis is calculated using the differences in average performance between the two variables.

The 90% confidence interval about the mean difference is obtained by calculating the variable:

$$u = t_{(0.95,df)} \times s_d \times SQRT(n)$$

Where:

$t_{(0.95,df)}$ = student's "t" value at 0.05 significance level and n-1 degrees of freedom
SQRT = Square root
n = Number of observations

The lower and upper limits of the 90% confidence interval is represented by the values:

$XBAR_d - u$ and $XBAR_d + u$

Where:

$XBAR_d$ = Mean of the difference between the HiTEC 3000 additive emissions and Howell EEE emissions

The results of the paired difference statistical calculations for the three emission types are given in Attachment 2C-3. The results indicate that the HiTEC 3000 additive does not have an adverse instantaneous effect on automotive tailpipe emissions. The average overall effect for HC and NOx is essentially zero while CO emissions show a favorable (decrease) effect for the HiTEC 3000 additive. The 90 percent confidence intervals for the three emission types include zero but none of the upper limits of the intervals exceed 10 percent of the Federal emission standards.

(2) Sign of Difference Test - This test assigns a "+" if the mean difference between the HiTEC 3000 additive emissions and Howell EEE emissions is positive and concurrently a "-" if the difference is negative. The number of pluses is counted and if the percentage is significantly higher than 50% of total observations, then the HiTEC 3000 additive would be seen to contribute to an adverse instantaneous effect on tailpipe emissions. The method used is a standard binomial test where the probability of a "+" = the probability of a "-" = 0.5.

The HiTEC 3000 additive does not cause an instantaneous effect on automotive emissions when the sign of difference statistical test is applied to the data. The maximum number of positive effects for the HiTEC 3000 additive in the nine automobiles was 4 which is even less than 50% of the nine observations. The minimum number of positive effects necessary to be statistically significant at the 90% confidence level in 9 trials is 7. The data are shown in Attachment 2C-4.

(3) Deteriorated Emissions Test - In this test the mean difference between the HiTEC 3000 additive and Howell EEE for each vehicle is added to the 50,000 mile certification value applicable to each vehicle to get a prediction of the waiver fuel emissions at 50,000 miles. The HiTEC 3000 additive is regarded as causing the vehicle to fail the emission standard if the predicted value exceeds the standard. The additive fails this test if the predicted number of failing vehicles is statistically significant.

The HiTEC 3000 additive does not cause an adverse instantaneous effect on automotive emissions when analyzed by the deteriorated emissions test. None of the mean effects exceed the federal emission standards when added to the 50,000 mile certification value applicable to each specific vehicle. The data for each vehicle/pollutant combination is shown in Attachment 2C-5. The 50,000 mile certification values for each vehicle were obtained from the Environmental Protection Agency.

Conclusion

Ethyl has done emission testing under Environmental Protection Agency guidelines to determine if the HiTEC 3000 additive causes adverse instantaneous effects to automotive emissions. Statistical analysis of the data, using three different testing procedures, indicates that the HiTEC 3000 additive does not cause adverse instantaneous effects to automotive tailpipe emissions.

Attachment 2C-1

AUTOMOBILES - INSTANTANEOUS EFFECTS

MODEL	C
V.I.N.	1G1JC5116JJ230682
ENGINE	2.0L J1G2.0V5XAG7
CATALYST	BPEGR/ORC

MODEL	G
V.I.N.	1G1AW51R7J6189377
ENGINE	2.5L J1G2.5V5TPG4 JAO-1C
CATALYST	BPEGR/ORC

MODEL	H
V.I.N.	1G2WJ14WXJF254703
ENGINE	2.8L J1G2.8V8XRZ8 JBO-1K
CATALYST	EGR/ORC

MODEL	I
V.I.N.	1G4HP54C0KH409549
ENGINE	3.8L K2G3.8V8XEB1 KBO-2O
CATALYST	EGR/ORC

MODEL	E
V.I.N.	1FAPP9592KW270441
ENGINE	1.9L KFM1.9V5FFF6
CATALYST	E9AE-9C485-8DV

MODEL	T
V.I.N.	1FABP52U9KG213904
ENGINE	3.0L SHM KFM3.0V5FEG0
CATALYST	E9AE-9C485-BAB

MODEL	F
V.I.N.	2FABP74FKX176846
ENGINE	5.0L 9HM KFM5.0V5HBF4
CATALYST	E9AE-9C485-BAZ

MODEL	D
V.I.N.	1B3B956326D216682
ENGINE	KCR3.0V5FBL5
CATALYST	4300655

MODEL	D
V.I.N.	1B30BU5630JD121070
ENGINE	KCR3.0V5FBL5
CATALYST	NOT AVAILABLE

Attachment 2C-2

INSTANTANEOUS EFFECTS DATA

All Models

CAR MODEL	HC, GM/MILE		CO, GM/MILE		NOX, GM/MILE	
	Clear	H3000	Clear	H3000	Clear	H3000
C	0.175	0.162	2.847	2.245	0.409	0.348
	0.155	0.166	2.193	2.413	0.281	0.343
	0.158	0.168	2.125	2.259	0.335	0.402
G	0.173	0.150	2.188	1.842	0.472	0.457
	0.177	0.158	2.683	1.775	0.514	0.446
	0.147	0.157	1.682	1.880	0.450	0.473
H	0.418	0.459	2.976	2.555	0.316	0.386
	0.396	0.442	2.881	2.337	0.310	0.356
	0.394	0.378	2.812	2.280	0.301	0.380
I	0.205	0.181	2.142	2.378	0.325	0.334
	0.190	0.176	2.180	1.971	0.356	0.321
	0.172	0.179	2.245	2.142	0.376	0.328
E	0.151	0.147	3.558	3.591	0.611	0.564
	0.159	0.151	3.984	3.859	0.625	0.556
	0.151	0.157	3.787	3.910	0.574	0.571
T	0.261	0.258	3.719	3.178	0.647	0.573
	0.303	0.241	3.323	2.867	0.593	0.655
	0.260	0.242	3.127	2.901	0.669	0.643
F	0.286	0.264	0.894	0.805	0.737	0.761
	0.303	0.273	1.079	1.065	0.704	0.739
	0.282	0.295	0.828	1.121	0.758	0.766
D	0.573	0.620	2.336	2.156	0.353	0.434
	0.553	0.606	1.822	2.169	0.414	0.504
	0.700	0.709	2.186	2.485	0.430	0.420
D	0.465	0.474	2.937	3.203	0.419	0.337
	0.513	0.456	3.529	2.975	0.393	0.355
	0.469	0.503	3.058	3.426	0.416	0.341

Attachment 2C-3

INSTANTANEOUS EFFECTS SUMMARY

Paired Difference Test

CAR MODEL	Mileage	Mean Difference, HiTEC 3000 - Howell EEE (gm/mi) HC	CO	NOx
C	24588	0.003	-0.083	0.023
G	30539	-0.011	-0.352	-0.020
H	18597	0.024	-0.499	0.065
I	21343	-0.010	-0.025	-0.025
E	11667	-0.002	0.010	-0.040
T	10513	-0.028	-0.408	-0.013
F	12959	-0.013	0.063	0.022
D	33936	0.036	0.155	0.054
D	30217	-0.005	0.027	-0.065
	Average Difference	-0.001	-0.123	0.000
	90% Conf. Interval			
	Lower	-0.013	-0.269	-0.027
	Upper	0.012	0.022	0.027
Upper Limit Exceeds 10% of Standard?		No	No	No

Attachment 2C-4

INSTANTANEOUS EFFECTS SUMMARY

Sign of Difference Test

CAR MODEL	HiTEC 3000 Effect HC	CO	NOx
C	+	-	+
G	-	-	-
H	+	-	+
I	-	-	-
E	-	+	-
T	-	-	-
F	-	+	+
D	+	+	+
D	-	+	-
P = Number of pluses	3	4	4

Number of P's necessary in 9 trials to be 90 percent confident that HiTEC 3000 has an adverse effect is "7". Therefore, the hypothesis that HiTEC 3000 has an adverse effect is rejected.

A-90-16

RESEARCH ON -

MANGANESE AND METABOLISM -

GROOTE EYLANDT, NORTHERN TERRITORY

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FOREWORD:

Research is being conducted, at the request of the Angurugu Community, Groote Eylandt, into the unusual disease conditions prevalent there.

This publication reports the proceedings of the conference held in Health House of the N.T. Department of Health, Darwin, on 11 June, 1987.

Thanks for support in this venture are due to the following organizations:

The Northern Territory Department of Health
The Angurugu Community Council
The Groote Eylandt Mining Company Ltd
The Church Missionary Society
The National Health and Medical Research Council
The Menzies School of Health Research, Darwin
The Department of Aboriginal Affairs
The University of New South Wales

All contributed in their own way to this production.

Joint editors:-

Prof John Cawte and Dr Charles Kilburn
Schools of Psychiatry, and Paediatrics,
University of New South Wales

REASONS FOR CONVENING THIS CONFERENCE

Chairman: Professor John Cawte

The colloquium was held at the Health Department of the Northern Territory, Darwin, on 11th June, 1987. The agenda was to share new information about the neurological disorders and possibly other related conditions affecting people at Angurugu, Groote Eylandt, where there is an unusual mineral ambience.

The colloquium host was Dr Keith Fleming, Secretary of the Northern Territory Department of Health. The convener and invited chairman was Prof. John Cawte of The University of New South Wales, stationed at Prince Henry Hospital, Sydney, but a long-time outdweller visitor-researcher.

The Angurugu Council, Groote Eylandt, and the Groote Eylandt Mining Company kindly made relevant personnel available to attend this meeting and provided the fares of some contributors travelling from outside Darwin.

This meeting was not designed as a medical conference in its usual sense. Medical information about these disorders was not felt, as yet, to be complete enough to generate that. However, enough information was available in early 1987 to convince both Prof. Cawte and the leading field researcher, Dr Charles Kilburn, that an informal gathering should be convened to share this information and to discuss the growing concern about these unusual disorders and their possible chemical environmental associations. Prof. Cawte and Dr Kilburn considered that they might be held remiss if they did not convene such a meeting, even while the present information is more contributory than completed.

Speakers were invited from the involved groups, ranging from the sufferers and their affected community outwards to consultant chemists and doctors. Speakers were asked to present their information in brief commentaries. Time was allowed for audience questions, discussion and for future planning designed to understand and to counter these grave conditions.

The meeting was, in effect, a sequel to an initial gathering held to discuss the outset of this research program, convened at the N.T. Department of Health, Darwin, on 1st December 1983. That meeting, which was then deemed confidential, had been entitled: *Possible Association of Manganism with the Groote Eylandt Syndromes.*

At that inaugural 1983 meeting Prof. Cawte presented two papers before lunch :

1. *Manganic Syndromes : Neurological; Psychiatric; Teratological; others.* Discussion followed.

   Manganese Toxicology: Findings since 1975: Human; Veterinary; Marine-Biological. Discussion followed.

After lunch the research proposals were discussed in terms of the findings up to that time; of suggested future work; of costs; and sources of funds.

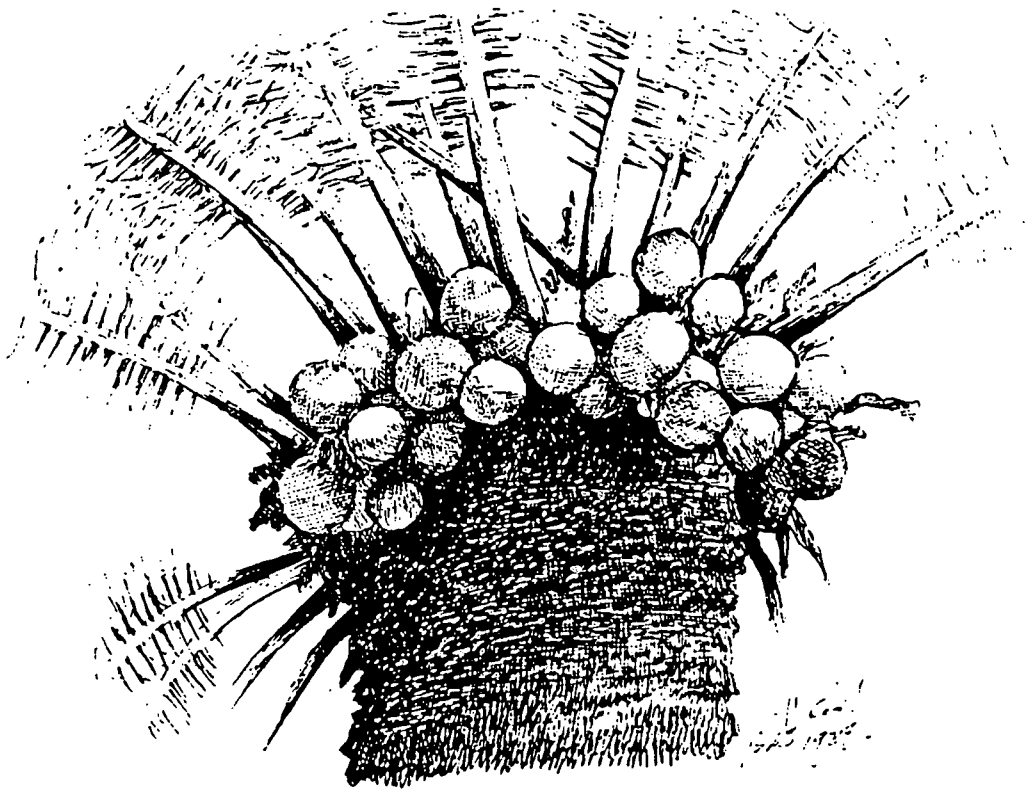
Immediately following that 1983 meeting, the Groote Eylandt Mining Company kindly donated $30,000 expense costs per year, for up to three years, and the Angurugu Community Council $10,000 per year, for up to three years. The former fund has been used chiefly for transport of skilled consultants to the distant site, and the latter chiefly for payments to local informants at the site helping the study.

Two years subsequently, in 1985, the NH&MRC awarded, on Prof.Cawte's application, a research fund that enabled Dr Charles Kilburn to undertake resident medical officer activity at Angurugu, Groote Eylandt, including a control study at Galiwinku, Elcho Island, N.T. Dr Kilburn also registered as a higher degree candidate at the University of New South Wales.

The present (1987) meeting was designed to review findings (especially clinical and chemical) since 1984, facilitated by the above financial support. The donors are thanked, together with members of the N.T. Department of Health and other organisations who have assisted. A tribute is paid to these parties in the Chairman's *Introduction of Participants* at this meeting.

After the June 11th 1987 colloquium, the contributing speakers were invited to draft their observations, which had been hastily prepared in most cases, in a form suitable for publication of *Interim Proceedings*,

including their references. These papers were typed by Ms Mary Hammill, compositor for the two education journals funded by the Commonwealth Department of Aboriginal Affairs: *The Aboriginal Health Worker* (Hon. Editor, John Cawte) and *The Aboriginal Child at School* (Hon. Editor, Dawn Muir). The final collection of material was printed, for limited circulation, by the University of Queensland Printery, St Lucia, Brisbane, including line illustrations by Aboriginal medical illustrator, Billy Reid.



A Burrawang (Cycad) in fruit, Groote Eylandt

COLLOQUIUM OUTLINE

Changes in the order of speakers were made on the day, reflecting speaker availability and other factors arising at the time

Chairman:	Introduction of participants; apologies and some tributes.
Mr Murubuda Wurramarba:	Views of the Angurugu Community Council, from its Chairman.
Dr Joan Ridley:	A Neurological Ethnic-Geographic Isolate (read from clinical paper by Professors Leslie Kiloh and John Cawte - not published in Australia).
Mr Graham Hams:	Findings from the Clinical Chemistry Laboratory at the Prince of Wales Hospital, Randwick, Sydney.
Dr Mark Florence:	Findings concerning the Manganese Ecology at Angurugu, from CSIRO at Lucas Heights, Sydney.
Dr Charles Kilburn:	Pediatric and Other Disorders at Angurugu.
Professor John Cawte:	What One Patient Taught One Epidemiologist (illustrated by video tapes of this patient under treatment).
Professor David Turner:	Anthropological Concerns.
Professor John Cawte:	The Angurugu Syndrome: Should the Community Consider Relocation?
Afterwords for the Conference:	Press Release; Paper reports; Notes by the Hon. W.C. Wentworth; Reports from Hawaii, and others.

CHAIRMAN'S INTRODUCTION OF PARTICIPANTS

Ladies and Gentlemen

Thank you for coming to an unusual gathering. I turn to you especially, Dr Keith Fleming, for hosting us all in your capacity as Secretary for Health and a few other services. I turn to you, Dr Ella Stack, for arranging this meeting in the Blue Room of Health House, providing our morning and afternoon tea and lunch, along with your usual interest in health problems. This is not a medical conference, but an associates' sharing of findings so far made respecting the Angurugu syndromes. It's a difficult issue. Dr Charles Kilburn and I, as chief workers in the field, felt that if we did not now call a meeting, we could be criticised for failing to communicate a problem that is hard to counter, and one in which the usual solutions do not apply.

Today's program has been altered several times during the past week. Some speakers are out of Australia. I could not confer with Dr Kilburn because he was out of contact with Sydney, being on Elcho Island. There are deficiencies today but at least we can all share the major points. We can conduct a medical conference in two or three years, my own estimate of the time needed for a full account, given enough support and funding on the way.

First, some apologies. Our early clinical worker, Professor Leslie Kiloh is having his Festschrift in Sydney today. He wanted to come to Darwin but I persuaded him that he'd better stay at home on this occasion. Dr Bill Webster, our hardworking embryologist exposing gravid rats to manganese, is overseas. So is Dr Ivor Dreosti, the expert on manganese, alcohol and superoxide dismutase at Adelaide's CSIRO. Dr Kilburn and I have consulted him in his manganese studies, which I hope Dr Florence, of Sydney CSIRO, will mention today.

It was Mr Clyde Holding, the present Minister for Aboriginal Affairs, who suggested that I should convene this meeting. We are fortunate to have with us his distinguished predecessor, the first Minister for Aboriginal Affairs, Hon. W.C. ("Billy") Wentworth.

We are grateful that we have a representative group of our Angurugu friends, who first asked me to study this problem years ago. We conferred with many more of them on Groote Eylandt yesterday. Today their group is led by Mr Murubuda Wurramarba, the Chairman of Angurugu Community Council. Also present is the Town Clerk, Bobby Nungamudjba, who spoke on this subject in Canberra with me a month or two ago. My friend, patient and chief helper is here. I will dwell later on what he has taught me. I am delighted that my dear Damiya is here today. She is the senior of the female health workers at Angurugu. We visitors slept at the Health Centre last night, and helped Damiya during a night disturbed by ills ranging from infection to compound fracture of the ulna.

The N.T. Department of Health is, of course, well represented here. I'm most grateful for the response of the Secretary, Dr Keith Fleming, whose words by phone to me in Sydney linger firmly in my mind. He just told me, "I'll do anything I can to help in this matter." He has given us hospital accommodations, use of a hire car, and is even asking me to lecture on Pablo Picasso tonight at a small barbecue at his (Keith's) home. A masochist for punishment, obviously, Dr Fleming.

It is good once more to meet with some Territorian medical friends. I've known the work of Dr Kerry Kirke over many years in The Centre. He's here as Assistant Secretary for Health Advancement, with responsibilities for Aboriginal health. Dr John Hargrave and I must have had Christmas dinners together after all the Hansen's disease he managed, ten years in a row, at the home of Rev. Harold Shepherdson and his wife Ella, at Elcho Island. It is good to see here Professor John Mathews, of the Menzies School of Health Research, who has such responsibilities for the future of health here, and who takes a special interest in this study. Also Dr Joan Ridley, an old psychiatric colleague of Professor Kiloh (I believe another Northumbrian) and myself.

I had dinner with Mrs Margaret Sheridan at Gove two nights ago. It's good to see her here, as Regional Director of East Arnhem Health. I rarely come to Darwin nowadays since I receive such support from her and her predecessors in East Arnhem Land during my medical invitations by those communities. Margaret knows all the best places to eat in Gove,

I am deeply relieved to find that Dr Mark Florence, outstanding trace element expert from CSIRO, Lucas Heights, has made it today. CSIRO researchers know a lot more about minerals than do medicos, and Mark has some crucial findings to offer us today in two talks that he is offering on behalf of himself and his Adelaide CSIRO Colleague, Dr Ivor Dreosti. Indeed, without the CSIRO findings on manganic ambience at Angurugu, I doubt if we should be holding this meeting today. Our sincere medical thanks to CSIRO and Dr Florence.

I have been travelling in the company of an old friend, Mr Don O'Rourke, First Assistant Secretary of the Programs Policy Division of the Department of Aboriginal Affairs in Canberra. Don wanted to look at the patients of whom we speak in their home setting at Angurugu. So did our other travelling companion, Mr Peter Moyle, of the Aboriginal Health Branch of the Commonwealth Health Department in Canberra. The Angurugu people were pleased to greet them.

From the Church Missionary Society I bring you the good wishes of Bishop Clyde Wood, who has always been interested and will try to be here later today. Two C.M.S. workers of Angurugu deserve our special thanks. Mary Harris (Mrs Eves) cannot be here today, but it was chiefly her concern, as a social worker, that first attracted our attention to this illness, as Dr Ridley's opening paper will describe. Mr Lance Tremlett, as C.M.S. Manager at Angurugu, has given us endless support and encouragement and, with his wife Gwen, hospitality over many dinner tables. Only yesterday Lance was showing us the famous old Mission garden, which we now know to be saturated with manganese, along with its plants that the people ate so much in those days.

I feel bound to pay a tribute to the remarkable group of C.M.S. research missionaries at Angurugu who have helped us in our work - Judith Stokes, Julie Waddy and, most of all, Dulcie Levitt now retired in Sydney, a botanist who periodically visits me at my hospital to talk about plants and people of Groote Eylandt. Our findings could offer Dulcie a new chapter in the next edition:

We welcome some guests from the Groote Eylandt Mining Company Pty Ltd, led by the manager, Mr Sergio Fuenzalida who, after being operations superintendent succeeded the previous manager, Mr Trevor Tennant, who

provided us with financial help some years ago. The Company's speaker today is Mr Alan Wright, a public relations officer who has always been deeply interested in the Anindilyakwa people, many of whom have worked for the company. I also see Mr Clive Thurlway, who is responsible for environmental interests of the company, and others. All have been helpful to us. We don't see here a previous employee, Mr Jack O'Hare, who retired on the Eylandt down at Yimbagwa, in a caravan. Jack is in Casuarina Hospital having surgery for his hip. I'll call on him tomorrow. Jack is not only welcoming to me on my too rare visits, but full of information about early times. We value Jack and wish him successful recovery.

Of my B.H.P. colleagues, I particularly welcome on everybody's behalf, Dr Robert Hart, head of the Division of Health and Safety for that company. I have been seeing Bob on and off over the years and I have found him realistic and experienced. My only objection to him is that he lives in Melbourne, when he is not overseas as he often seems to be. I decided to go to Melbourne BHP headquarters to see him last week, as he was not able to keep his appointment to see me in Sydney. He is accompanied by his epidemiologist colleague, Dr Michael Fett.

From my own group of hospital consultants in Sydney we welcome the neuro-chemist, Graham Hams. Graham makes some striking discolosures today. With his newly installed atomic absorption spectrometer, he has disproved a contention that one commonly finds in older books, that tissue manganese is not measurable in humans, for the most part. Graham has demonstrated high levels in the blood of most of our neurological patients, which we never expected to find. It helps us!

Of my other colleagues, the neuro-pathologist, Prof Bruce Warren was here a month ago. As yet we have no autopsy studies but we hope that Bruce will rectify this. The community has accepted Bruce's role. The neurologist, Dr Keith Lethlean will be up here next month with his myogram recorder and assistant, Dr Heather Johnson.

I really want to thank all the nurses who have assisted us over the years, but there are too many, so I'll restrict my thanks to Rachel Jordan, one of the first sisters to help me ten years ago. I saw Rachel yesterday in her new capacity with the AIDS problem. We are all in her debt.

Groote Eylandt has known many famous anthropologists, from Norman Tindale, whom I knew of old at the South Australian Museum (whenever he was there) and C.P. Mountford. I suppose the most famous is Donald Thomson, whose remarkable public achievements one can read about in Dr Nicolas Petersen's well illustrated book, *Thomson in Arnhem Land*. Indeed, Thomson, more than any other, created precious Arnhem Land as a Reserve for its people. I have also met Prof Fred Rose, now in East Berlin, who had the foresight to include photographs of residents in his book. But today we are lucky to have with us the leading anthropologist of the present day, Prof David Turner of Toronto. He will be speaking to us shortly.

I have to apologise to my normal Arnhem Land hosts of Elcho Island, where I have spent most of my vacations for 20 years as an anthropologist physician. I have attended them medically and studied their healing and their mourning, as well as their religion, and their latest craze of drinking Kava from Fiji. I am involved in advising the Western Australian Government on that drug substance - we are convinced it is a drug, not a food - but I have had to sacrifice Elcho interests to attend to Groote Eylandt of recent years. I'll go back "home" when I can. Meantime, our child specialist who is working on Groote under my NH&MRC grant, Dr Charles Kilburn, recently carried out his control study on Elcho, and no doubt represented me well. You'll hear today how we are lucky to have such a sincere and balanced specialist as Dr Kilburn. I'm grateful that he'll move to Darwin after the grant is over and hopefully continue his work on Groote Eylandt as a consultant.

Giving my grateful thanks to you all for contributing today, I can only apologise if I have missed someone I should recall. You are all deeply valued in the pursuit of this mysterious and tragic disease and the unusual ambience in which it occurs.

A final word for the most valuable consultant who is not here today, because he is at home in Quebec. Professor John Donaldson is in my opinion the world's authority on the effects of manganese on the nervous system. He visited me last year when I was a guest at the Center for Advanced Study in the Behavioral Sciences at Stanford, California, and he taught me and Dr Kilburn last December in Australia about the vagaries of this element in the nervous system. We await his new article on this subject in the forthcoming issue of *Neurotoxicology*. We wish you were here today, John, to talk about the 140° longitude neurological disorders.

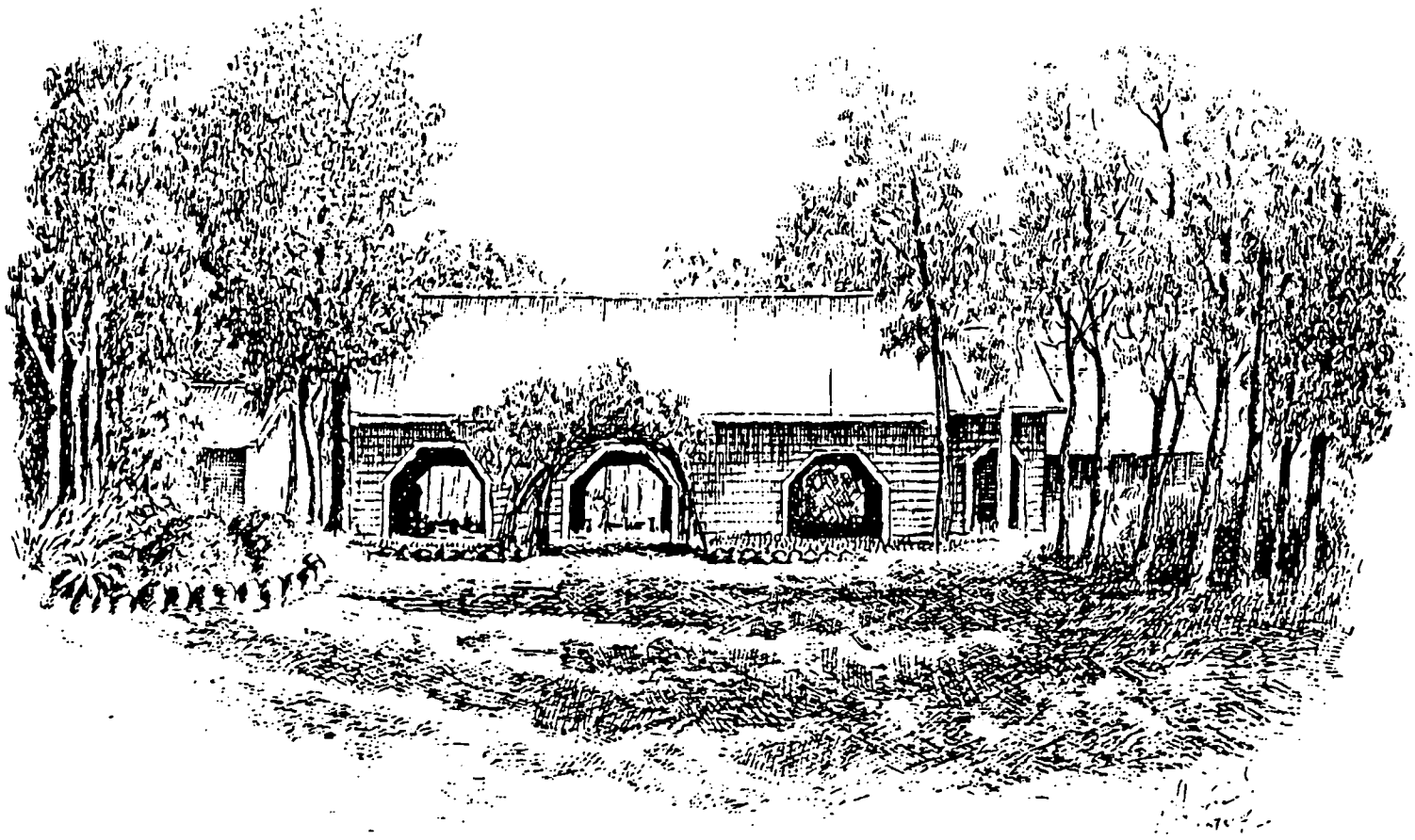
CHAIRMAN, ANGURUGU COUNCIL

Mr Murabuda Wurramarba, Chairman of Angurugu Council, spoke briefly about the concern of his people over their strange diseases. He mentioned that they had asked Dr Cawte to give his opinion some years ago. Since then many advisers had visited. Finally Dr Charles Kilburn who had lived with them and carried out important medical work, particularly with children.

Mr Murabuda said that his people were anxious that the research go forward to a successful conclusion. The disease must be controlled to make the people strong and happy. He emphasized that the people did not want any public attention, fuss or trouble. They just wanted their disease understood and relieved.

He thanked today's experts for coming to this meeting.

A Groote Eylandt shoreline



The church of the Church Missionary Society, at Angurugu.

A NEUROLOGICAL ETHNIC-GEOGRAPHIC ISOLATE ON GROOTE EYLANDT*

L.G. Kiloh and J.E. Cawte#
University of New South Wales

Groote Eylandt, which curiously retains its Dutch name though probably discovered by the Portuguese, is the largest island in the Gulf of Carpentaria in the North of Australia. Its bearings are latitude 14° South and longitude 138° East. Together with a small cluster of Aborigines on one of the nearby islands and on the mainland, the total Aboriginal population is about 1100.

On our way back from Elcho Island we visited Groote Eylandt briefly in 1977 and met Mary Harris, a social worker who had spent a number of years on the island. Mary Harris was disturbed by the number of Aborigines with neurological disorders and drew our attention to them. In the short time available we saw a number of the patients and returned a year later accompanied by Dr Keith Lethlean and Dr Graeme Morgan. With the help of Mary Harris and the nursing sisters we were able to identify thirteen definite and three probable cases. We studied them in more detail than was possible during our earlier hurried visit and gave some consideration to possible etiological factors.

To summarise the first findings (Kiloh *et al.* 1980) there were seven cases showing features of a motor neurone disease, two with only lower motor neurone involvement and five with the additional lateral sclerosis. One of the latter had shown only lower motor abnormalities on our first visit. In four of these seven cases abnormalities were observed by the mothers soon after birth. Most of these patients also showed a striking degree of hypotonicity with very lax ligaments. One of this group whom we did not see had died several years before, having developed a bulbar palsy. There were six patients with a curious mixed picture showing cerebellar features and pyramidal tract involvement. Four showed a variety of supranuclear and internuclear ophthalmological paralyses and three some muscle wasting. In addition, there were three

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*From K.M.Chen & Y.Yase (Eds) 1984: *Amyotrophic Lateral Sclerosis in Asia and Oceania.* National Taiwan University.

#This paper was read at the Conference by the Darwin psychiatrist, and colleague of the writers, Dr Joan Ridley.

Aborigines with lax ligaments whom we thought had a mild and probably non-progressive ALS-type syndrome. Of thirteen definite cases, one showed a mild dementia and in another this diagnosis was queried. A mild degree of parkinsonism was also queried in two patients.

It is unfortunate that we have had great difficulty in obtaining funds to investigate the Groote Eylandt population further. One of us (J.E.C.) has managed to look in briefly several times on his journeys to and from Elcho Island. We have kept in close touch with one of the important members of the Aboriginal Council who happens to be one of the patients. About two thirds of the cases appear to have progressed. Two have died, but even had we been there at the time it would probably have been impossible to have obtained autopsy material. One new case has been located with cerebellar and upper motor neurone features.

It might be worth adding that other peculiarities have been noted in the Groote Eylandt inhabitants. In one family ten of twelve siblings have died, nine in early childhood. One, who survived to the age of five years was never able to walk. In two other related families there is a remarkably high incidence of heart and renal disease and of twelve siblings, four have died in late adolescence or early adult life and two others are affected. There is also hearsay evidence of a psychiatric syndrome unusual in Australian Aborigines, in which the patient is subject to unexpected episodes of rage and aggression - something between amok and the episodic dyscontrol syndrome. Our informants indicate that in women it occurs in the first trimester of pregnancy.

We considered that the syndromes, although varying widely, were likely to be examples of a polymorphous condition having a common etiology.

At the time of our first visit we were impressed by the strong familial nature of the illnesses and we thought that they were likely to be genetic. In a small closed community of this kind everyone is related in some degree to everyone else and Dr Graeme Morgan found great difficulty with his genetic studies. However, strongly against a primary genetic basis was the fact that in the 1920s the population of Groote Eylandt had been studied separately by Dr Tindale and Dr Rose, both of them competent and observant anthropologists. Neither of them referred to any neurological disease. Rose photographed every member of the population but his findings

were not published until 1960; no indication of these disabilities appears. Furthermore, none of the missionaries drew attention to the condition, nor do the Aborigines themselves have any tradition - and established sorcery explanations - of such a disorder.

The possibility that neurotoxins derived from cycad nuts or cassava was considered but rejected. The most striking ecological feature of the population of Groote Eylandt is that most of them live in the middle of a large manganese deposit and are surrounded by open cut mining activities and dumps of crushed ore. In the principal of their two villages, lumps of black manganese oxide can be picked up in the streets and at any time a thin film of black dust can be wiped from furniture and other exposed objects. The local river from which the water supply is derived runs across a bed of exposed manganese ore. The other Aboriginal village in which two cases were identified lies on the opposite side of the island and has no nearby manganese deposits. However, there is much movement between the two areas. The three mainland patients are also distant from the major manganese deposit but again mobility does occur and furthermore they live on the edge of Blue Mud Bay, originally so named by Flinders, Captain Cook's successor as a cartographer. The colour was later found to be due to manganese. Amongst Aboriginal bark paintings those from Groote Eylandt can easily be identified at a distance by their extensive use of black pigment - a colour available to other Aboriginal communities only as charcoal.

At the time of our visit we considered the possibility that manganese was responsible for the genesis of the neurological abnormalities. At that time our knowledge of manganese intoxication was limited to the acute and chronic syndromes suffered by miners in Egypt and Chile, which are dominated by extrapyramidal syndromes. These differ markedly from from those presented by the Groote Eylandt Aborigines. At the same time, we did not overlook the fact that up till 1942 the entire population lived beside Emerald River some 20 odd miles south of the manganese deposit. In that year their airstrip assumed strategic importance and was taken over by the Royal Australian Air Force. Perhaps not without justification, the community became concerned and moved the settlement up the coast to the next major water supply and established the village of Angurugu where most of our cases were found.

It is interesting to consider the birth dates and the times of onset of the sydnromes in relation to the move to Angurugu. Of the sixteen cases, five were born before the move and only two after the development of the mining operation. In none of the cases we know about did the syndrome appear before the move but in eight the symptoms began before the mine was opened.

We have carried out an intensive study of the literature on manganese and there appears to be considerable evidence from animal and veterinary studies that in addition to its effects upon the mature nervous system, manganese is capable of teratogenic effects perhaps directly, perhaps by interaction with other elements, or perhaps in association with protein malnutrition.

[Our early notes on these syndromes were made nearly ten years ago. Since then we have published several research papers describing our studies and we have established a research physician on the island. The recent findings of high levels of manganese in the blood of neurological patients and in the garden soil and plants of the village, will be outlined in today's proceedings. These findings certainly add interest to our early investigation].

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ANALYSIS OF MANGANESE IN WHOLE BLOOD

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A method for determining the concentration of manganese in whole blood was established in my laboratory during 1986.

The method utilised the laboratories' AA975 atomic absorption spectrometer which was equipped with the GTA 95 electrothermal atomiser (both manufactured by Varian Pty.Ltd. Mulgrave, Vic.) The analytical technique was a novel application based on a technique reported in literature in 1986.(1)

The spectrometer was operated in double beam mode and used a deuterium background correction facility. The furnace atomiser employed a solid pyrolytic graphite platform to reduce condensed phase matrix interference.

Samples for analysis were collected on Groote Eylandt by Charles Kilburn, as heparinised whole blood. The collection apparatus was 'rinsed' with patients blood prior to sampling for manganese so as to minimise contamination from the hypodermic needle. The samples were transported to the laboratory at 4^{o}celsius.

Within the laboratory, the samples were diluted to one fifth of their original concentration with manganese free diluent water. The diluted blood was mixed with a small volume of 70% w/w nitric acid (Univar, Ajax Chemical, NSW) and more water within the furnace atomiser. The temperature of the atomiser was increased slowly from 40^{o}celsius to 400^{o}celsius while maintaining a pure oxygen atmosphere over the sample. The atomiser temperature was then increased more rapidly to 800^{o}celsius after changing the atmosphere to pure argon. Gas flow was stopped and the sample residue atomised at 2600^{o}celsius. Atomic absorbance signals were measured as peak height.

The analysis was routinely calibrated with aqueous standards. Periodically, the parity between aqueous calibration and standard additions calibration on a low manganese concentration whole blood was ascertained.

The analysis showed ample sensitivity. Peak height absorbances ranged from 0.04 units to 0.12 units over the laboratory reference interval of 100 to 350 nanomoles manganese per litre of blood. This interval compares favourably with other workers' estimations of a reference interval (2,3,4.)

Background absorption during atomisation of whole blood samples can be an intractable problem. The combination of matrix modification, oxygen ashing and temperature profile used in this analysis both reduced the absolute size of the background signal to a manageable level and moved it temporally so that interference was minimised before the application of background correction. (fig.1)

Analysis of whole blood collected from eight neurologically affected Aboriginals from Groote Eylandt showed six individuals to have markedly increased manganese concentrations. Eight unaffected Aboriginals resident in the same area showed normal blood manganese concentrations (5).

DISCUSSION OF THE RESULTS

The technique as applied appears to indicate a possible association between elevated blood manganese and the occurence of the "Groote Eylandt Syndrome".

If the association is shown to be valid by further testing it maybe that these affected individuals have increased organ exposure to manganese through one or a combination of the following metabolic abnormalities:-

1) increased intestinal absorption of a normal manganese load
2) increased exposure to environmental manganese but a normal uptake.
3) decreased hepatic excretion of manganese

Future studies to verify or reject the association between elevated blood manganese and the neurological syndrome should include:-

1) some form of population survey or surveys of Groote Eylandt to accurately determine the local "normal" range of whole blood manganese levels.
2) comparison of results for affected and unaffected individuals to check for the association.
3) follow-up studies over a period of some months to identify varying exposure to manganese.
4) analysis of cord blood to determine the extent of in utero exposure.
5) manganese body balance studies

CONCLUSION

A method for analysing manganese in whole blood samples by atomic absorption spectrometry has been developed. The technique has good operational characteristics and shows excellent analyte and background signal separation.

Application of the method to a small sample of bloods taken from Groote Eylandt Aboriginals may indicate some association between elevated blood manganese and a neurological syndrome. This association has yet to be proved

Future studies should include a population survey to assess general exposure and individual response to environmental manganese.

It should be noted that this laboratory is able to carry out a small scale preliminary survey for no charge. However, should larger scale surveys or population monitoring be required (either by the Aboriginal community or by the Groote Eylandt Mining Company for its employees) some funding would be required to increase the laboratories analytical capacity.

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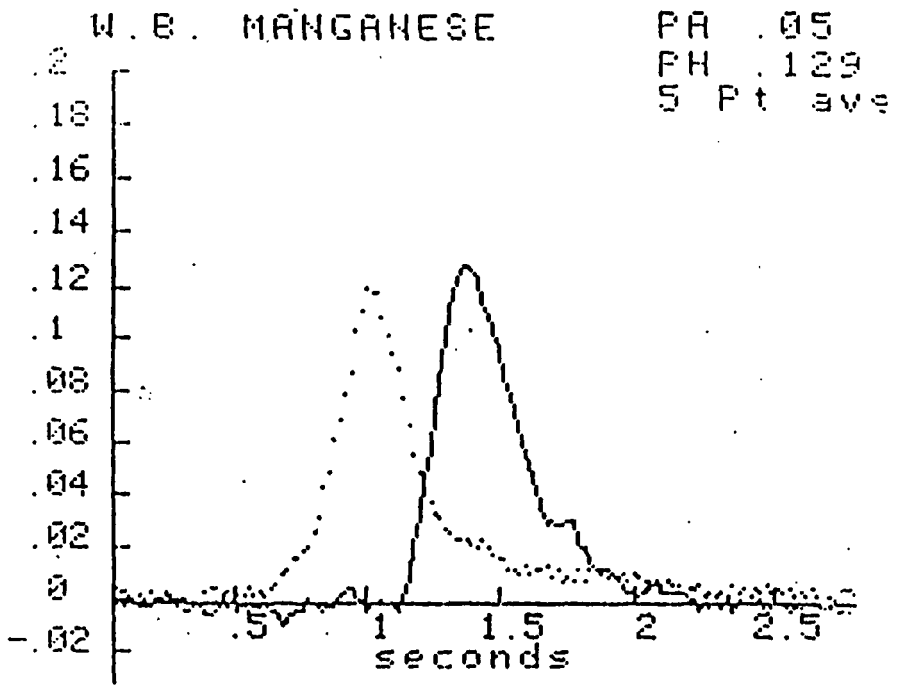
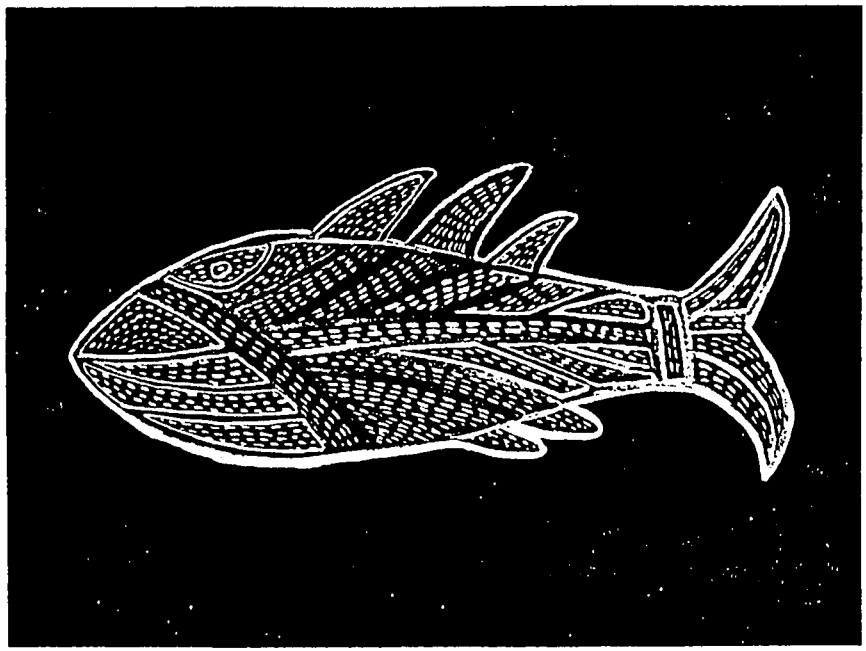


Fig.1 Detail of analyte (dark) and background (dotted) signals during the atomisation phase of the blood manganese analysis. The sample concentration was approxomately 300 nanomedes per litre.



The Barramundi
by
Kneepad
From *Time Before Morning* by Louis Allen, 1975.
Crowell Co., New York.
The Groote Eylandt style often features prominent figures in dashed lines on a background made black by manganese oxide rather than by charcoal.

Ecological Studies of Manganese on Groote Eylandt

T.M. Florence, J.L. Stauber and J.J. Fardy,

CSIRO Division of Energy Chemistry,
Lucas Heights, N.S.W.

1. Introduction

Most manganese salts have low acute toxicity, and manganese was thought for a long time to be one of the most innocuous of elements [1]. The long-term (chronic) toxicity of manganese was recognized later, as a result of neurological disorders with symptoms similar to Parkinson's Disease appearing in some manganese miners, particularly those in Chile [2].

Groote Eylandt has extensive and rich manganese deposits which are mined and provide a valuable export for Australia. The main Aboriginal village of Angurugu is situated in one area of manganese mineralization, with high soil and plant manganese. A small number of Aborigines have developed unusual neurological problems which are somewhat similar to those reported for miners suffering from manganese intoxication, and it was important to determine if these problems (the "Angurugu Syndrome") were associated with excessive manganese intake.

In this respect, an obvious question is: "If all the inhabitants of Angurugu are uniformly exposed to high levels of manganese, why are only 1-2% of the population affected?" This question can be answered on the basis of individual susceptibility. In the Chilean manganese mines, less than 5% of the miners developed chronic manganese toxicity; one miner may have been severely affected while his workmate, working beside him for the

same length of time, and exposed to the same concentrations of manganese in air, showed no toxic symptoms whatsoever [3]. This phenomenon of individual susceptibility has been observed with other metals such as lead, mercury and beryllium, and also with tobacco smoking. Most people know of a relative or friend who has smoked heavily all his life yet has not developed lung cancer or any of the other smoking-related diseases. Others, with a much lower tobacco usage, succumb quickly. The differences in ability to cope with toxicants is believed to result from individual variations in uptake rate and clearance rate of the toxicant, and the inducibility of enzyme systems which detoxify the foreign compound. In case of manganese, the most important factor is believed [4] to be the differences in the excretion ability of the liver and kidneys.

This study was undertaken to establish manganese concentrations in the environment and diet of Groote Eylandt Aborigines, and to compare the results with world average concentrations.

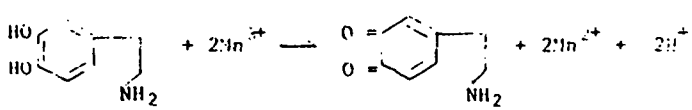
2. Toxicology of Manganese

Donaldson and co-workers [5] have shown how the neurotoxicity of manganese could arise as the result of Mn(II)/Mn(III) catalysis of dopamine oxidation in the brain. Our own studies at Lucas Heights indicate that the relevant reactions are:

$$Mn^{2+} + O_2 \longrightarrow Mn^{3+} + O_2^{\cdot -} \qquad (1)$$

$$Mn^{2+} + O_2^{\cdot -} + 2H^+ \longrightarrow Mn^{3+} + H_2O_2 \qquad (2)$$

net, (1) + (2): $2Mn^{2+} + O_2 + 2H^+ \longrightarrow 2Mn^{3+} + H_2O_2$ (3)



(4)

dopamine dopamine quinone

Reaction (1) proceeds only in the presence of a manganese(III)-complexing ligand (such as pyrophosphate, citrate or xanthine) and dopamine. The products of manganese and dopamine oxidation, ie, hydrogen peroxide and dopamine quinone, are strongly neutrotoxic. Catalase, the enzyme responsible for destroying H_2O_2 is low in the brain, and superoxide dismutase, the enzyme which dissociates superoxide radical ($O_2^{\bar{}\bullet}$), is unevenly distributed [6]. Manganese(II), however, efficiently catalyzes the dissociation of $O_2^{\bar{}\bullet}$. Superoxide radical, normally considered a dangerous species in biological systems, is nevertheless essential in the brain for the synthesis of the neutrotransmitters, norepinephrine and serotonin [7]. A certain level of manganese may also be essential to participate in vital redox reactions, but too high a concentration could lead to serious toxic effects.

The neurotoxic effects of excess manganese may be, (i) reduction of dopamine concentrations, (ii) production of toxic dopamine oxidation products (quinones and semi-quinones), (iii) production of hydrogen peroxide (iv) destruction of superoxide radical. Other metal ions, such as Cu^{2+} and Fe^{2+}, can also catalyze these reactions, but they are usually tightly bound in enzymes, and not free to participate in reactions such as (1)-(4).

3. Blood Analyses

The determination of manganese in blood is of little use for the diagnosis of chronic manganese poisoning [3]. Manganese miners with severe symptoms of manganism, after removal from the workplace, usually had normal manganese-in-blood concentrations [3]. On the other hand, apparently healthy miners, working in the mine, had high blood manganese. Manganese in the human body is characterized by two half-lives of 4 and 40 days, so blood manganese can only give an indication of recent exposure, and provides no information about the body store of manganese [2]. Nevertheless, for equally exposed individuals, high blood manganese may

indicate those with enhanced uptake mechanisms and/or deficient clearance mechanisms.

Results for catheter-collected (Jan 1987) blood from Groote Eylandt inhabitants are given in Table 1. The manganese values were determined by Mr Graham Hams, Clinical Chemistry Department, Prince of Wales Hospital. Neutron activation analysis was also carried out at Lucas Heights on some of the bloods and, in general, good agreement was obtained.

The average blood manganese (μg/L) for the four groups (Table 1) were: GEMCO workers (omitting No. 1), 8.4; Caucasians in Angurugu, 7.3; affected Aborigines (omitting No. 7), 36.1; unaffected Aborigines, 18.9. The normal range for manganese in blood is 6 to 12 μg/L, with a mean (Sydney) of about 8.5 μgMn/L. The Caucasian inhabitants of Groote Eylandt have blood manganese values close to this mean, but Aborigines unaffected by the Angurugu Syndrome have double the Caucasian blood manganese, and those affected, four times. The affected Aborigines also had low hemoglobin (normal range 12-18 g/dL) and low ferritin (normal 25-150(F), 75-260(M) μg/L). Therefore, in addition to high blood manganese, they have a low iron status (anemia).

One sample of cord blood from an Angurugu baby delivered in Gove had 41 μgMn/L, even though the mother's blood was normal (7.2 μgMn/L) and the concentration of manganese in the placenta was low (0.12 μg/g dry wt.).

4. Factors that Exacerbate Manganese Toxicity

The following factors are known to increase the toxic effects of manganese [8].

(a) Low iron(anemia). Iron and manganese have a similar uptake mechanism; anemic individuals have enhanced absorption of both iron and manganese, and are known to be more susceptible to the toxic effects of this element [2].

(b) Chronic infections. Infections cause an increase in the production of H_2O_2 and free radicals in the body, putting greater strains on the ability

of the cellular and extracellular antioxidants to scavenge these toxic substances, already produced in excess by the catalytic action of excess manganese. Some natural antioxidants are vitamins C and E, glutathione and free radical-dissociating enzymes.

(c) High alcohol intake. The metabolism of ethanol liberates H_2O_2 and free radicals, and depletes the liver of the antioxidant glutathione.

(d) Low dietary calcium. Manganese can displace calcium from nerve endings and hence disrupt the central nervous system. This is more likely to happen in an individual with high manganese and low calcium status.

(e) Low zinc status. Zinc protects sulfhydryl groups (e.g., glutathione) from oxidation by H_2O_2 and free radicals. These compounds are therefore more susceptible to manganese toxicity when zinc is depleted.

5. Manganese in sweat and urine

Three Aboriginal brothers from Angurugu, one deemed as severely affected by the Angurugu Sydrome, one moderately affected, and one unaffected, were brought to Sydney for medical tests. In all three cases, the urine (<0.3-1.1 ugMn/g creatinine) and sauna sweat (3-11 ugMn/L) were within the range found for Lucas Heights controls.

6. Chelation Therapy

The three brothers mentioned above were treated at Prince Henry Hospital with calcium ethylenediaminetetraacetic acid (EDTA) in an attempt to remove excess body manganese. Urine analysis showed, however, that after correction for the manganese blank in the Ca-EDTA, no manganese was removed by the chelation therapy.

7. Manganese in hair

Hair concentrates trace elements from blood supplying the hair follicle, and hence manganese in hair should be an indicator of blood levels of this element. In addition, since scalp hair grows at the rate of 1.0-1.5 cm/month, changes along the length of a hair should be a record of changing blood concentrations during that period.

This ideal situation is complicated by external contamination of the hair - from dust, shampoos, and hair treatment which may add or subtract elements from the hair. Manganese is one of a group of elements known to increase along the length of a hair even when blood concentration of the element is constant. This was believed to be due to increased environmental exposure to the element as the hair grew, but our research has shown that the increase results from sweat elution. Sweat glands near the hair root produce sweat which travels up the hair, dissolving manganese from dust particles on the hair, and concentrating the element towards the tip of the hair. Under these conditions, hair is acting as a wick or chromatographic column, with sweat as the eluant. This phenomenon occurs only with those elements that form lipid-soluble complexes with sweat. To overcome this exogenous effect, a plot of manganese concentration in washed hair versus length from scalp was constructed for each hair sample, and the graph extrapolated to zero length. This "zero-length" manganese concentration should represent the hair manganese unaffected by external factors.

A summary of results is shown in Table 2. All Groote Eylandt inhabitants had hair manganese values higher than Sydney residents, probably as a result of a continuous, albeit low, intake of excess manganese. Aborigines had much higher manganese in hair than Caucasians, although there was no significant difference between affected and unaffected subjects.

8. Manganese in Air and Water

Manganese in air in Angurugu (average about 5 $\mu g/m^3$) is 100 x the Sydney and European average (Table 3). However, manganese in air would contribute only about 0.1 mg manganese/day to the intake of an Angurugu resident, and so would be an insignificant percentage of total intake unless, of course, respired manganese is particularly toxic. Manganese in Angurugu air is well below the occupational limit of 200 $\mu g/m^3$.

Manganese in the village tapwater and the Angurugu River appears to vary seasonally, up to 10 x the Sydney and world average. However, manganese from this source would amount to, at the most, 0.3 mgMn/day, and so would be insignificant. Calcium in the Angurugu River (0.2 mg/L) was very low, only 0.01 x world average.

9. Manganese in Traditional Food Sources

Some traditional ("bush tucker") food samples were collected from the Angurugu old village garden areas (used extensively before 1970) and analyzed for manganese (Table 4). Some of the foods were exceptionally high in manganese, and contained 3-100 x the world average for these items. A peeled yam, for example, had 660 μgMn/g (fresh weight), compared with 5 μgMn/g in a Sydney carrot. On this basis, one 20-g yam would supply 13 mg of manganese, or 3 x the recommended daily allowance (RDA) of this element (4 mg).

Boiled ("billy") tea extracts about 5 times the amount of manganese from tea leaves as does brewed tea. One litre of billy tea would contain 6-7 mg manganese.

10. Manganese in Soils

Soil samples in the old Angurugu garden areas (Table 5) were exceptionally high in manganese (up to 100 x world average) and very low in calcium (0.04 world average). Soil samples taken near Aboriginal houses in Angurugu were about 10 x world average in manganese. Umbakumba soil was very low in manganese.

11. Manganese in Organs of Experimental Animals

Organs of animals captured near Angurugu varied considerably in manganese content, but some were particularly high, e.g., thymus, adrenals, spleen, and the brain (Table 6).

12. Conclusions

I have reached the following preliminary conclusions from these

1. Angurugu Aborigines have a high intake of manganese, but the actual amount is very difficult to determine. Air and water contribute insignificantly to their total intake but, because of their "close to the earth" living, relatively poor hygiene, and the high manganese content of Angurugu soils, ingested manganese may be considerable.

2. Before the store was opened in 1970, Angurugu Aborigines used about 80% "bush tucker" in their diet. This bush tucker consisted largely of vegetables and fruit grown in the garden area, which has extremely high soil manganese. Their dietary manganese from this source alone could easily have been 100-200 mg manganese/day (25-50 x RDA). At present, bush tucker constitutes only 10-20% of their diet, and may not be as significant as damper cooked in the earth and billy tea.

3. There is no known way of measuring, in vivo, the total body burden of manganese. Blood and hair only indicate manganese in readily exchangeable pools such as soft tissue, and chelation therapy appears to be ineffective. The availability of autopsy samples would help considerably.

4. Anemia, chronic infections, high alcohol intake, low dietary calcium, and low zinc status are factors that exacerbate manganese toxicity, and are commonly found in Angurugu Aborigines.

5. Hair analysis suggests that Caucasians in Angurugu, and GEMCO workers, have a higher manganese intake than non-exposed persons, but much less than the Aborigines.

13. Future Work

I believe that the following work is necessary to clarify the question of excessive manganese exposure in Angurugu.

1. Additional blood analysis. Although it is well established that blood manganese analyses indicate only very recent exposure, they may pinpoint individuals with a defective clearance mechanism and/or enhanced uptake mechanism. Every attempt should be made to collect cord blood and hair

manganese is concentrated across the placenta. Control cord blood samples would also have to be collected because little is known about the normal manganese concentration in cord blood.

2. Autopsy samples can be rapidly and non-destructively analyzed by neutron activation analysis. As many as possible should be collected.

3. An attempt should be made to estimate the bioavailability of manganese in Angurugu soils. Standard procedures could be used for this.

4. Hair analyses of people who have lived on Groote Eylandt and left should be carried out to determine if, and how rapidly, manganese in hair decreases when exposure to this element is removed. If levels remain high, it may mean that hair can be used as index of body burden of this element.

14. References

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TABLE 1 BLOOD ANALYSES ON GROOTE EYLANDT INHABITANTS

Subject	Mn µg/L	Fe µg/L	Hb g/dL	Ferritin µg/L
1. GEMCO workers				
1	22.3	503	16.6	233
2	6.0	454	15.5	280
3	9.9	420	14.2	124
4	9.1	407	14.9	146
5	12.6	498	16.1	165
6(F)	10.7	364	13.3	87
7(F)	6.9	406	14.5	158
8	6.3	495	16.8	93
9(F)	7.7	391	14.1	53
10	6.3	448	15.9	125
2. Caucasians in Angurugu				
1(F)	5.8	419	13.8	-
2	4.9	413	15.1	110
3(F)	8.8	361	12.1	30
4(F)	9.6	359	12.7	67
3. Affected Aborigines				
1(F)	38.7	331	11.3	28
2(F)	36.3	297	10.4	5
3(F)	15.7	356	11.4	0.3
4	42.3	191	8.9	11
5	42.1	-	-	-
6	41.2	-	-	-
7(F)*	9.3	381	13.1	367
4. Unaffected Aborigines				
1(F)	25.5	351	-	-
2	9.9	472	16.4	354
3(F)	16.8	336	12.3	34
4	17.6	452	15.0	96
5	24.9	-	-	-

*Lived in Umbakumba for 15 years.

TABLE 2 MANGANESE IN HAIR

Subjects	Mean manganese, µg/g	
	Scalp*	Pubic
Sydney	0.5±0.2	1.3±0.5
GEMCO workers	2.2±0.8	3.0±0.4
Caucasians in Angurugu	2.5±0.7	7.9±4.1
Unaffected aborigines	15±5	21±5
Affected aborigines	9±3	23±7

*Extrapolated to zero length.

TABLE 3 MANGANESE IN AIR AND WATER

Sample	Angurugu	Sydney	World Average
Tapwater, µgMn/L	4.3(8/85) 70(1/87)	5.8	-
Angurugu River, µgMn/L	27(8/85) 97(1/87)	-	8(for rivers)
Air, µgMn/m^3	23(3 m from road) 1.2(10 m from road)	0.05	0.04(European)

TABLE 4 MANGANESE IN TRADITIONAL FOOD SOURCES COLLECTED FROM OLD GARDEN AREAS*

Sample	µgMn/g fresh weight	
	Angurugu	Sydney
Fish, Angurugu River	36	0.3
Oysters, Mud Cod Bay	0.25	0.05
Yam, young	657	5**
Yam, old	484	5**
Citrus fruit	0.85	0.3
Banana	79	1.5
Billy tea	6.7	-

*U.S. intake: range 2-9 mgMn/day, mean, 3.7 mg/day.
**Root vegetables.

TABLE 5 MANGANESE IN SOILS

Source	Manganese, % dry weight*
Near Angurugu houses	0.2-1.2
Angurugu road	4.1
Old orchard	1.4
Old vegetable garden	4.6
Cassava plantation	0.11
Banana plantation	4.2
Mud Cod Bay sediment	0.33
Emerald River settlement	0.15
Umbakumba	0.002

*World average soil has 0.05% manganese.

TABLE 6 MANGANESE IN ORGANS OF EXPERIMENTAL ANIMALS

Organ	Manganese, µg/g, fresh weight			
	Angurugu Melomys*	Sydney rat	Groote dog	Sydney dog
Thymus	2.5	0.24	-	0.49
Adrenals	4.2	-	0.17	0.05
Spleen	1.7	0.24	0.27	0.33
Cerebellum	1.1	0.45	1.4	0.50
Choroid plexus	1.5	0.59	8.1	0.90

*Bush rat.

Early contact at the Mission. The deformity of the arm and hand of the woman on the left is particularly evident in the photograph from which Billy Reid worked - (Cole, K., 1975: *Groote Eylandt*, p.15).

NEUROLOGICAL DISORDERS ON GROOTE EYLANDT

Dr Charles Kilburn*

Unusual and poorly explained neurological disorders affect between one and two percent of the Aboriginal population of Groote Eylandt. Congenital malformations and psychiatric disturbances have also been linked to these Groote Eylandt syndromes (Cawte 1984) Rich manganese deposits in and around the main Aboriginal settlement of Angurugu have led to speculation about the possible role of manganese in these disorders.

For the past two years I have been resident on Groote Eylandt, employed by the University of New South Wales under a National Health and Medical Research Council grant to investigate these conditions. This research has been in conjunction with laboratory studies carried out by Dr Mark Florence of the C.S.I.R.O. at Lucas Heights Sydney, Dr William Webster at Sydney University and latterly Graham Hams at Prince of Wales Hospital Sydney. Professor John Cawte was responsible for instigating and coordinating this research.

Firstly I would like to discuss some results pertaining to birth defects, then to describe the neurological illnesses and finally to discuss some recent blood manganese findings.

In an effort to determine if there is an increase in congenital malformations I reviewed the birth records of all children born to Aboriginal parents resident on Groote Eylandt from the first of January 1975 till the first of January 1985. This cohort was also physically examined as part of a population survey. Another Aboriginal community was studied in the same way as a control group. There was no significant difference in either the incidence or the spectrum of of congenital malformations found. The incidence of stillbirths was also studied with the rationale that stillbirths may represent the severe end of a spectrum of teratogenic effects. These statistics were obtained retrospectively from local health centre records and community census information. Data were cross checked against hospital records. While cross checking is not fully completed, the incidence of Groote Eylandt stillbirths, 12 in a total of 286 births both live and stillborn, is not significantly higher than the 19 in a total of 579 of the control group. The general health status of these two communities was comparable, as evidenced by similar infant mortality rates (40 per 1000 Groote Eylandt; 39 per 1000 control). This should control for the effects of general health on the incidence of stillbirths and congenital malformations.

Next I would like to describe the neurological illnesses unusual to Groote Eylandt. My enquiry into the neurological status of the Groote Eylandt Aborigines has proceeded along two lines: an examination of affected individuals and a comprehensive survey of the childhood population.

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Aboriginal children born since 1/1/75 have been neurodevelopmentally assessed coincident with the community survey for birth defects. Since the Groote Eylandt Aborigines are in many respects still tribal and have had limited contact with the outside world until relatively recently, any discussion of these results requires a socially and culturally appropriate control group study for comparison. I have just finished an examination of such a control group but have not completed analysing the data. Therefore I will confine myself to a description of affected individuals.

Informants drawn from both Aboriginal and European sections of the community.were asked to list people with problems of weakness, gait, coordination and ocular movements. These are the major manifestations of the Groote Eylandt disorder being studied. After physical examination and study of their medical records those individuals whose disorders were explicable by other diagnoses (e.g. cerebrovascular accident, cerebral palsy, trauma, etc) were eliminated. This left a group of patients most of whom segregated readily into two clinical syndromes. This group includes most of the patients described by Kiloh *et al* 1980).

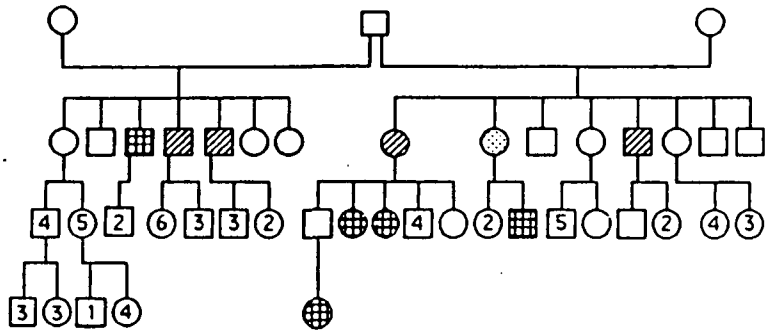
One patient, an Angurugu inhabitant who earlier described the onset and progression of his symptoms, exemplifies one of these groups of cases. This group, characterised by ataxia and oculomotor disturbances, falls into the clinical grouping of spinocerebellar degenerations. Five individuals are currently affected by this disorder, four of them sharing one father. The other case is unrelated and currently lives at Numbulwar though he spent his school days and early working life on Groote Eylandt. The onset of symptoms is insidious and occurs in the fourth or fifth decade. Unsteadiness is the usual presenting complaint. Gait is ataxic and wide based, with arms outstretched seeking furniture or walls for support. When turning, staggering is prominent. Other signs of cerebellar dysfunction are present including incoordination, dysmetria, intention tremor and dysdiadochokinesis of both upper and lower limbs. Nystagmus, both at rest and on upward gaze, is present in the four more severely affected individuals, as is limitation of upward gaze. Convergent gaze is diminished in all cases.

The second syndrome is characterised by muscle wasting and weakness. Clinically it is a form of motor neurone disease, with a prenatal or at least early childhood onset. Weakness and wasting is predominantly distal and affects the lower limbs more than the upper. Muscle tone is generally low, although two of the older and more severely affected cases have increased extensor tone in the lower limbs. Deep tendon reflexes are brisk in most cases, especially in the lower limbs. Even in those cases with profound weakness and wasting, reflexes are generally surprisingly spared. Foot deformity (talipes equinovarus and/or pes planus) is universal and often noted at birth, strongly suggesting a prenatal onset. Spinal deformity (kyphosis or kyphoscoliosis) is also present in all but the most mildly affected. Striking laxity of the ligaments and small joint hyperextensibility is a prominent feature in most cases, demonstrated by spontaneous swan neck deformities of the fingers on extension and passive extension through > 100 degrees at the metacarpophalangeal joints. This suggestion of connective

tissue disorder is supported by a curious soft, almost plasticene-like skin texture and mild skin hyperextensibility, but without evidence of abnormal scarring or easy bruising. Some of those affected with this syndrome are the children or grandchildren of individuals with spinocerebellar degeneration. The others with this syndrome are unrelated to anyone with spinocerebellar signs but can be grouped into a separate extended family pedigree. The inheritance shows a familial clustering but does not comply with a Mendelian pattern (Figure 1).

FIGURE 1.

A



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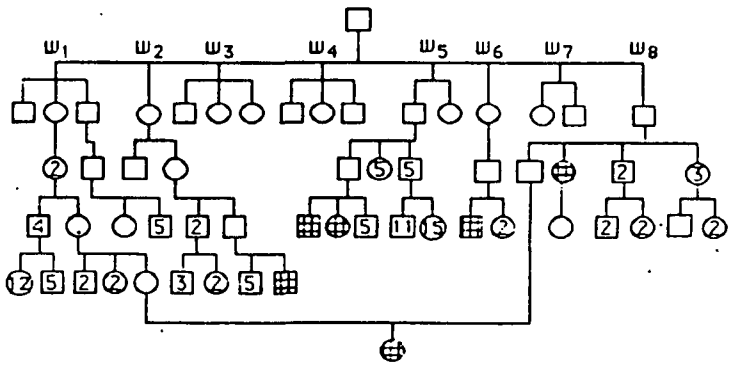

A. Condensed pedigree of family 1.
B. Condensed pedigree of family 2.
Enclosed numerals represent numbers of offspring.
In B, "W" with subscript indicates wife number. None of the progeny of the offspring of wives 3, 4 or 7 are affected and so have been omitted.

Unaffected male Unaffected female
Case with amyotrophic syndrome
Case with ataxic syndrome
Unclassified neurological disorder

These two syndromes are linked by one pedigree which includes cases of both types, and an overflow of clinical manifestations between the two syndromes. One case, now deceased, presented a fusion of the features of both syndromes.

Finally I would like to discuss some recent blood manganese results. Earlier efforts at estimating manganese status of the Angurugu population had concentrated on analysis of scalp hair. This was because we hoped scalp hair may have provided a way of looking at more than just immediate manganese exposure. Serum manganese estimations are not only technically difficult, as evidenced by the wide range of normal values quoted in the literature (Halls and Fell 1981), but together with whole blood levels are also said to be of no value in diagnosis of manganese toxicity. As Dr. Florence has indicated, scalp hair manganese assays were increased amongst Angurugu inhabitants, but probably were still only representative of the rapidly turned over pool of manganese.

In November 1985, three brothers from Angurugu were transferred to Prince Henry Hospital, Sydney, for neurological investigations. Two were affected with the spinocerebellar disease and the other was a normal sibling. As a new assay for whole blood manganese had recently been developed at Prince of Wales Hospital, blood was collected from all three brothers. The results showed that the two affected cases had elevated whole blood manganese levels (640, 630nMol/L) while their unaffected brother had a normal level (390nMol/L). On receipt of these results blood was collected from a further five people affected by the motor neurone type syndrome and from four unaffected Angurugu Aborigines. The unaffected people were selected from a group who had had hair samples analysed and were two individuals with high hair manganese levels and two with normal to low levels (for Angurugu). Blood was also collected from a total of fourteen non Aboriginals, four resident at Angurugu and ten employees of Groote Eylandt Mining Company living at Alyangula. Including the results of the three brothers tested in Sydney a total of twenty six specimens have been analysed for blood manganese (Tables 1 and 2).

Analysis of these results shows that gross elevation of whole blood manganese levels is confined to Aboriginal residents of Angurugu who have neurological disease. Five of the seven cases with neurological disease tested show this elevation of whole blood manganese. None of the five unaffected Aborigines from Angurugu have high blood manganese. Although these numbers are too small to draw firm conclusions and the control group was not selected totally at random, there is a strong suggestion of an association between elevated blood manganese levels and the neurological disorder. This must be of concern, particularly as manganese is a recognised neurotoxin. While the neurological disorders found on Groote Eylandt do not correspond exactly with that classically described in manganese miners, the similarities are apparent. Yase (1972) found elevated manganese levels in spinal cord tissue taken from ALS patients from Guam and the Kii peninsular

in Japan, where high levels of this metal are present in soil and water. Recent studies have also found an increase in manganese levels in the spinal cords of patients dying with motor neurone disease (Miyata *et al* 1983 and Mitchell *et al* 1986).

TABLE 1.
Results of whole blood manganese analysis.of Angurugu Aboriginals

Sample#	Blood manganese (nMol/L)	Sex	Status
1	640	male	spinocerebellar
2	630	male	spinocerebellar
3	710	female	motor neurone
4	660	female	motor neurone
5	170	female	motor neurone
6	285	female	motor neurone
7	770	male	motor neurone
8	465	female	unaffected
9	180	male	unaffected
10	305	female	unaffected
11	320	male	unaffected
12	390	male	unaffected

TABLE 2.
Results of whole blood manganese analysis.of Non-Aboriginal residents of Groote Eylandt.

Sample#	Blood manganese (nMol/L)	Sex	Residence
1	160	female	Angurugu
2	175	female	Angurugu
3	105	female	Angurugu
4	90	male	Angurugu
5	405	male	Alyangula
6	110	male	Alyangula
7	180	male	Alyangula
8	165	male	Alyangula
9	230	male	Alyangula
10	195	female	Alyangula
11	125	female	Alyangula
12	115	male	Alyangula
13	140	female	Alyangula
14	115	male	Alyangula

It is unlikely that the elevated manganese levels found in neurologically affected cases is directly causal, as whole blood manganese probably reflects only very recent exposure. However it may be a marker of an abnormality in manganese metabolism which could predispose to manganese accumulation. If this is so, it should allow identification of those at risk. Another interesting observation is that even unaffected Aborigines living at Angurugu have higher blood manganese levels than Europeans living at either Angurugu or Alyangula. This suggests that some factor related to Aboriginality or an Aboriginal lifestyle predisposes to an accumulation of manganese in whole blood.

In summary I could demonstrate no evidence of increased congenital malformations or stillbirths occurring on Groote Eylandt when compared to another Aboriginal community of similar health status. There is however a strong suggestion of an association between elevated blood manganese levels and neurological disease. This must be cause for concern, particularly in view of the known neurotoxic potential of manganese. I am about to conduct a case control study in an attempt to clarify this apparent association.

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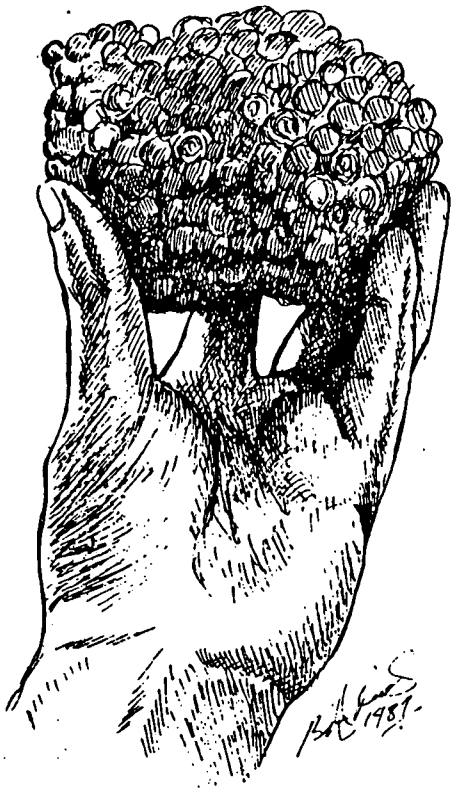

A nugget of manganese ore in the form of pisoliths, obtained in the village

WHAT ONE PATIENT TAUGHT ONE EPIDEMIOLOGIST

Professor John Cawte

What is epidemiology?

Epidemiology, according to my Webster's dictionary, is 1: a science that deals with the incidence, distribution and control of disease in a population (as of animals or plants); 2: the sum of the factors controlling the presence or absence of a disease or pathogen; 3: the ecology of a disease or pathogen.

For the mental health epidemiologist such as I, none of these definitions is really adequate. We can't study what are generally called diseases, though some of us give patients classifications that sound like diseases, such as mania, depression and schizophrenia. Most members of my profession consider this too narrow an outlook. When we study patients we look successively at a range of processes in the mental life, in the body, in personal relationships, and in the physical environment. We call our viewpoint holistic, rather than categorical. I teach students what I'd call "perignosis" rather than "diagnosis". That's what psychiatry is about.

Our work is complicated and time-consuming, and we are easily criticised by epidemiologists who want to ask more specific questions than psychiatrists usually ask, making the human problem more simple. It would be pleasant if it were! I learned psychiatric epidemiology in part from a famed Canadian teacher at Harvard in the 195[illegible] Alexander Leighton, who developed those historic studies of what he called "The Character of Danger" of a Nova Scotia community which he named *Stirling County*, and another he called by its correct name *Midtown Manhattan*. Some of his techniques can be found in my own book on this subject dealing with Australian tribal people, entitled *Cruel, Poor and Brutal Nations* (1972). This is the name that the Dutch explorer, Jan Carstens, gave to the folk of Mornington Island, south-east of Groote Eylandt. For today's purposes I only wish I had studied "The character of danger" at Groote Eylandt. We

should then be further ahead. I mention this work to show that I studied mental health epidemiology among tribal people, and that it is a different problem from what many more urban epidemiologists imagine. For a start, you have to be something of a linguist, an anthropologist, as well as an effective doctor, who wins their confidence through his relief of their sufferings. One must therefore smile, a little sadly, when experts who do not attempt these skills tell us from an office how to run our business.

We have worked on Groote Eylandt too briefly. For me it's mainly on vacations. The first thing I learned about this disease complex that affects them is that you can't classify it easily. It's not clearly spelled out nor defined in any of the books that I have read. I decided that I had to start with a single patient, offer a continuing relationship, earn his cooperation and then put together all the facts one could learn in those four domains in which he lived : his mind, his body, his society and his environment. Any of the four might help, none could be disregarded. Some facts fade and others grow bolder as time rolls by.

The single patient who has helped me most in defining this unusual problem has been kind enough to come here to this meeting today for you to meet him and hear his tale of illness. He has let me run some tests and trials to define his illness. I shall tell you about these tests, made in the hope that they will clarify. In doing this, he has shown courage, hope, persistence and cooperation - all stirling values in his make-up as a man. His English, and rapport with me is good, partly because he had training as a motor mechanic in Adelaide. He welcomes our team to Groote Eylandt not just for himself, but because of his concern for the future of his family and the other persons affected. There is a nobility about his suffering that deserves some recognition and esteem.

This man is 45 and has been increasingly affected for about 10 years. We shall not go into details of his symptoms here, as we have reported them several times in the literature. Neurologically, he is affected by an upper motor neurone disease - A.L.S., causing stiff movements, and by oculomotor disease causing poor vision and distance judgment, and by cerebellar disease causing poor balance and a wobbly gait on widely-spaced feet. He cannot walk backwards; he would fall. In addition to his spino-cerebellar disease, some judges would note signs of bulbar

palsy. We have neurological test findings that confirm these obvious signs and symptoms but this is not the place to detail them.

He has been admitted to my hospital in Sydney, which locals call The Coast, on several occasions. Firstly he came with a group of other patients with similar conditions. Then he came with his wife and children, whom we lodged in the hospital's "motel" near the chapel, overlooking beautiful Little Bay and our own private beach surrounded by cliffs. Last November he came with two full brothers, an older one 55 and a younger one 35. The older is also affected but the younger is not. At weekends the four of us usually went driving - for example down the South Coast to see our old missionary friend, Mary Eves. So much for his inpatient status.

Let me indicate the various findings which he was the first patient to reveal. The same tests and studies might be offered to other patients. I cannot accept the criticism that Dr Kilburn and I have failed to carry out all these tests on everyone. Give us the time and the staff, and we will. When we have done all that, maybe we can conduct epidemiology in the sense our critics suggest.

HIGH BLOOD MANGANESE LEVELS

This patient was the first of the cohort to show a high level of manganese in the blood. Last November his level was found to be 640 nanomols (n mols). Mr Graham Hams today discusses the atomic absorption spectrometry he uses for trace elements in the Clinical Chemistry Department of the Prince of Wales Hospital at Randwick. At the same time, the level of brother "Senior" with a similar but milder neurological syndrome was found to be 630 namomols. I once freed "Senior" of a police charge of being drunk in a vehicle. I wrote a letter indicating that his staggering at that time was, in my opinion, probably due to this neurological disorder. The blood manganese level of young brother "Junior", who is unaffected, is much lower, at 320 nanamols.

But all these levels surprised us. The literature did not suggest they would be found. It has two half-lives, both fairly short, as Dr Florence tells us, and blood manganese only suggests recent exposure. Dr Kilburn conducted further blood tests in the vicinity, with similar findings in most of the neurologically affected patients, though normal

in others, including some Europeans. He will conduct more, at the Community's request, when he has time. Mr Graham Hams in Prince of Wales Chemistry is waiting for the samples.

Two neurologically affected subjects who live at Umbakumba do not show high levels of blood manganese. Apart from current non-exposure (the metal is not ambient there) I don't know how to explain it. Perhaps it is lack of exposure to manganese latterly? Perhaps it's a difference in susceptibility? - metabolic? - nutritional? - Family? - Other? We don't know. But look at my tables, 1 and 2.

Table 1

Manganese found in whole blood in 26 individuals at three townships of Groote Eylandt
(Note: initials have been coded to protect identity)

	Initials	Age	CNS Disease	Blood Mn. n mol/l
Aborigines in Angurugu	I.M.	Adult	Yes	630
	L.M.	Adult	Yes	640
	T.M.	Adult	No	390
	S.N.	Adult	Yes	710
	S.B.N.	Adult	Yes	660
	Q.S.	Infant	Yes	465
	H.X.	Adult	No	180
	T.N.	Adult	No	305
	U.M.	Adult	No	320
	W.M.	Child	Yes	770
Caucasians in Angurugu	M.L.	Adult	No	105
	D.L.	Adult	No	90
	K.X.	Adult	No	160
	M.E.	Adult	No	175
Aborigines in Umbakumba	E.C.	Adult	Yes	285
	N.C.	Adult	Yes	170
Caucasians in Alyangula	U.U.	Adult	No	405#
	B.X.	Adult	No	110
	C.K.	Adult	No	180
	K.O.	Adult	No	165
	H.B.	Adult	No	230
	E.O.	Adult	No	195
	M.C.	Adult	No	125
	N.U.	Adult	No	115
	L.X.	Adult	No	140
	E.T.	Adult	No	115

Note: Trace metal chemists have advised us of two reference ranges for this metal: 100-350 n mol/L, and 100-500 n mol/L.
This surprisingly high level, in an apparently well person, was replicated and found to be very similar on the second test.

Table 2

The time incidence of disorder of movement (limb weakness, cerebellar and eye movements and connective tissue disease) on Groote Eylandt, 1945 - 1985

Case No	Pedigree	Year of Birth	Sex	Onset	Weakness	Ataxia	Ocular Move-ments	Connective Tissue Disease
1	2	1982	F	Child	+++	-	-	++
2	2	1977	M	Child	+++	-	-	++
3	2	1975	M	Child	+	-	-	-
4	1	1972	F	Child	++	-	+	+++
5	1	1968	F	Child	+++/++	-	+/-	-
6	2	1962	F	Child	++/+	-	-	+++
7	1	1961	F	Child	+++	-	+	-
8	2	1960	M	Child	+	-	-	+++
9	1	1958	M	Adol	++	+	++	-
11	2	1956	F	Child	++/+	-	-	++
11	1	1945	F	Adol	++	-	-	-
12	1	1943	M	Adult	+	++	++	-
1	1	1940	M	Adult	+	+++	+++	-
14	1	1938	M	?Child	++	+	-	-
15	1	1939	F	Adult	+++	-	-	-
17	1	1935	F	Adult	+	++	+	-

CHELATION

Our friend here is also the first patient whom I tried to chelate. Many metals, of which lead is perhaps best known, can be removed from the body by administering substances which have an affinity for them, and are then excreted. I could have chosen penicillamine as chelating agent, but after a study of the literature I chose calcium versenate or Ca:EDTA.

Here is a summary from his hospital discharge summary of 3rd December, 1986:

> Other investigations were undertaken in conjunction with Dr Mark Florence of CSIRO. They included treatment with intravenous calcium EDTA in an attempt to boost manganese excretion in the urine. Results indicate that this indeed does promote manganese excretion and may have a place in prophylaxis of this condition for young Groote Eylandters.

Unfortunately for this hypothesis, Dr Florence later reported that the agent calcium EDTA itself may have been suspect of containing trace contents of manganese. Next time I shall get the agent tested by him beforehand, or use penicillamine. It should be noted, too, that Dr George Cotzias, the American investigator, found that chelation, even if it is valid, may offer little clinical comfort to established (chronic) sufferers.

CARBIDOPA ADMINISTRATION

He is also the only patient to have had Carbidopa, a form of L-Dopa. The substance was first given by this American, Dr George Cotzias in 1968 to affected manganese miners in Chile. It is still given to patients affected there by motor neurone disease, as it reduces their symptoms through its action on the neuro-hormonal profile. More recently (Guidice, 1986) found it to help rigidity and spasticity patients after head injury - voice and movement. They benefit from increased dopaminergic function and improve in consciousness. (Mary Ann Guidice is a Detroit neurologist). Dramatic advances were made in neuropsychiatry in the 1960s from improved knowledge of the neurotransmitters. In more recent times, increasing attention is given to the trace elements, especially manganese, in the production of catecholamines.

We did not then know that he had a high blood level of manganese, though we knew that he had a high hair level, through Dr Florence of CSIRO. I gave him *Sinemet* tablets containing Levodopa 250 mg and Carbidopa 25 mg. I made videotapes of his walking before, during, one week after, and two weeks after these treatments. I named the films "Red", "Blue" and "White" respectively, corresponding to the colour of his jackets. I convened a group of qualified neurological and psychological colleagues to appraise the performance on 10 parameters. These judges were not told of his condition, nor its treatment. "After treatment" scores showed great improvement. T tests showed $p<.001$. I shall now show you these films: see for yourself.

After *Sinemet* he walked faster and recovered his balance quicker after lurching.

After the first tape the patient was given a low dose of *Sinemet*, which was gradually increased over the next few weeks to a maximal dose of $\frac{1}{1}$ tabs q.i.d. The further two tapes were taken in the same setting, at weekly intervals. The patient felt improved, saying that his joints were less weak. He walked with less falling.

In my view there was also an improvement in his mental state. He was quicker in speech and thought. There was a lifting in mood, conversation and activity, with more attention and more smiling.

We discontinued Carbidopa treatment after he returned home, believing that he was again exposed to manganese. As well, this is not an easy treatment to supervise. Raising the dopamine by this means may deplete amino acids methionine and cystine, which should be supervised. Also, when this treatment is given for those affected by manganese, it is not usually given to those with structural damage, but only to more acute cases. This is the recommendation made by the WHO Health Criteria, anyway.

At least we studied how he responded to these two recommended approaches, chelation and L-Dopa. Manganese-exposed patients should be removed from the site of exposure. It might have seemed wise to most observers to suggest that he, and other neurologically affected patients, move to an unexposed site. Alas, for him it is HOME! We shall consider this problem later today.

Meanwhile, this single patient compelled us to study whatever was known about the role of manganese in health. For this we thank him. As suggested, possibly the best library source used to be IPCS - International Program on Chemical Safety, Environmental Health Criteria 17. MANGANESE, W.H.O. Geneva, 1981. Its contents might be indicated here, for those interested. It extends over 100 pages, including references. Other good sources will be cited in *References*.

ENVIRONMENTAL HEALTH CRITERIA FOR MANGANESE